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VOLUME IV *September, 1956* NUMBER 9

PANEL DISCUSSION ON HEART DISEASE*

Moderator†: CHARLES T. STONE, SR., M.D.
Panelists†: HARRY GOLD, M.D.; DAVID LEHR, M.D.; ROBERT L. LEVY, M.D.; HAROLD E. B. PARDEE, M.D.; WESLEY E. PELTZER, M.D.; AND CHARLES F. WILKINSON, JR., M.D.

MODERATOR STONE: It is unnecessary to make extended comment before a geriatrics group as to the importance of heart disease in older subjects. It is always a problem that we have with us, and it is the purpose of this panel to bring you the views of the participants with respect to certain aspects of heart disease.

Inasmuch as atherosclerosis is perhaps the most important cause of heart disease in older individuals, I am going to call upon Dr. Wilkinson to develop for us his thoughts with respect to the pathogenesis of atherosclerosis.

DR. WILKINSON: The current concept that many of us have as to the development of atherosclerosis is based not only on experimental data, but on pathologic changes seen in human beings. At the risk of oversimplification, I would say that there is, first, *an inherent defect in the artery*, a metabolic defect that

* Conducted at the Graduate Symposium on Geriatric Medicine, American Geriatrics Society, New York City, November 30 and December 1, 1955.

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may be inherited. Because of this defect, there is a *piling up of lipids* in the intima of the artery. This later develops into what is called *a yellow or lipid plaque.* The earlier this plaque is in point of time, the more nearly its composition resembles that of the circulating lipids in the blood. As the plaque grows older, the composition changes, and there is a higher concentration of cholesterol, which is less metabolically labile than other fats.

As the plaque grows older, a certain amount of fibrous reaction takes place. Eventually, the plaque develops into what is called by Holman "a pearly plaque." It is white, rather than yellow. At this point, experimentally, the plaque is nonreversible.

All of this can take place without clinical symptoms. *Clinical symptoms* may be associated with either a *lipid plaque*, which is reversible (at least in the experimental animal) or a *pearly plaque*. The objective in the treatment of atherosclerosis should be to prevent or reverse the lipid plaque, because, from a pathologic as well as an experimental point of view, the process is nonreversible when the fibrous reaction has taken place.

Even plaques that have not changed for many years may be a cause of trouble. Paterson and other pathologists have shown that hemorrhage may occur behind or into the plaque. The plaque may, by causing a decrease in the amount of blood that comes through the artery, cause anoxia or the gradual development of a clot.

Even though atherogenesis is not actively taking place, the clinical signs of atherosclerosis may develop—coronary occlusion, angina pectoris, or cerebrovascular accident.

It is extremely important to realize that we are treating the clinical symptoms that are the result of the atherogenic process. The clinical symptoms are the recognizable effect of a process that is probably going on in all of us.

If we paired off the men and the women in this room, age for age and, relatively, weight for weight, there would probably not be much difference in the amounts of atherosclerosis present in the two groups. The fair sex would, however, be very fortunate as to the distribution of their atherosclerosis.

There are other things that cause atherosclerosis to be more prevalent in some groups than in others. Hypertension is an important factor. The rate at which the body can clear the blood stream of a fat load is important. Secondary hyperlipemia, which may be associated with several conditions, (*e.g.*, diabetes and hypothyroidism), is important. Probably, hypercholesterolemia is important but, to my mind at least, it is far less so than the other factors mentioned.

MODERATOR STONE: Thank you, Dr. Wilkinson.

We learned during our medical student days that the first thing to do when a patient comes in is to take a history and make a physical examination.

Dr. Gold, have you some ideas with respect to the value of, and the risks in taking histories and making physical examinations when dealing with older patients?

DR. GOLD: The advantages of a good history and physical examination are

well known. There is some question as to what we do with the information gleaned from the history and the physical examination and what we tell the patient.

In the routine physical examination in which one is hunting, not for what is normal in a person, but for what seems to be abnormal, one runs the risk of giving rise to illness that does not exist.

Among elderly people, one not uncommonly finds abnormal electrocardiograms, abnormal blood pressures, murmurs, and vascular alterations. If we observe the patients periodically over a protracted period of time, we may find changes in these areas.

It is important to know about these changes. The question arises as to what to tell the patient about them. A real danger lies in the possibility of stirring up in the patient inherent fears about his health. I should like to suggest that the most important aspect of this periodic examination is not the finding of a change in the electrocardiogram or in the blood pressure, or in any of the other specific points of the history and physical examination, but rather, the total evaluation of the individual's performance.

On the basis of my experience with elderly people, I believe that there is a tendency to overtreat, overdoctor, and overmanage them. The things that the doctor says to the patient, based upon the abnormalities detected in examination, can have subtle effects.

DR. LEVY: May I say a word?

MODERATOR STONE: Yes.

DR. LEVY: I should like to amplify what Dr. Gold has said. First, with respect to the electrocardiogram; those who have an opportunity to take repeated records will find, in older persons, that from time to time changes occur which suggest that small arteries have become occluded. Often such changes are found in the absence of a history of any acute episode. Sometimes, if you inquire closely, you may find that there has been a bout of what is called indigestion or a short, sharp pain in the chest.

As Dr. Gold has stated, such changes, if emphasized, can bring unnecessary anguish of mind to the patient and his family. We know from the work of Blumgart, Schlesinger, and their associates, that the process of gradual occlusion of coronary arteries and arterioles often takes place in the absence of clinical evidence that alterations have occurred. These observers have found hearts at necropsy, with closure of all three main arteries, in patients with no history of infarction or anginal pain. Such changes must be evaluated in terms of the patient's functional capacity and general condition.

The same is true of other findings, such as an elevation of systolic blood pressure, which is often merely a manifestation of stiffening of the arterial system.

MODERATOR STONE: I am sure these gentlemen do not want you to believe that you should not take a complete history and make a careful physical examination. I believe I can summarize what they have attempted to say by reminding you of the old statement that there is a patient that has the disease as well as a disease that has the patient.

Perhaps second in importance in heart disease in older patients is hypertension. Dr. Peltzer, would you like to speak on that phase of the subject?

DR. PELTZER: Dr. Stone, I realize that even within the panel I am in trouble, and I expect that controversial questions from the floor will follow what I have to say.

I should like to start by saying that almost since the invention of the sphygmomanometer, physicians in general have been aware of the fact that high blood pressure present over a period of many years is a serious condition in most individuals. Before we had effective remedies, it was acceptable to treat the complications of hypertension. However, strange things have happened to our point of view, now that we have extremely potent remedies.

A large segment of the medical profession has taken the attitude that hypertension is really not such a bad condition, and perhaps the patient should learn to live with it. This attitude has developed as a result of the notable fact that many persons with significant hypertension live for thirty, forty or fifty years and die of causes unrelated to their hypertension.

Dr. Levy told you that systolic hypertension is not of great importance, but I am willing to be put on record as favoring the treatment of all patients with *significant* hypertension by means of reasonable therapeutic measures. Now, to try to rectify my position with those of more conservative thought, I think that overdosage is a large part of this problem.

I should like to explain what I mean by *significant* hypertension. I do not mean the patient whom you have been following for six years or six months, who one day has a systolic pressure of 170 but who previously has had pressures within a normal range, 160 or 150; neither do I mean the patient who occasionally has a diastolic pressure of 110. On the other hand, when you find on repeated examinations that a patient has a systolic pressure of 170 or even 160 and a diastolic pressure close to 110, you are, I think, obligated to treat him.

In the field of geriatric medicine, more than anywhere else, you have a field of endeavor and active therapeutic agents that will bring great good to your patients and, thereby, prove gratifying to you.

I shall now discuss what I consider reasonable treatment for these patients. There would not be much controversy on this panel in regard to treating individuals with organic deterioration of the heart or of the eye grounds, who have had a cerebrovascular accident, or who show signs of kidney dysfunction. I think that the members of the panel would agree with the premise that whatever seems necessary and justified to correct the hypertension should be carried out, for otherwise the disease will end the patients' lives.

The differences of opinion seem to arise over the question of whether or not to treat patients (symptomatic or asymptomatic) who have elevated blood pressures. They are the patients that I am interested in treating for prophylactic value.

I give such a patient up to a maximum dosage of reserpine and include, as a reasonable therapeutic measure, hydralazine (Apresoline) in a dosage up to 400 or 600 mg. per day. That is not too high a price to pay for moderation of the blood pressure.

Before using the ganglionic blocking agents, it should be shown that the patient has organic deterioration because of his blood pressure.

I have three charts that I should like to show you. Figure 1 illustrates the course of the blood pressure in a woman, now 71 years of age, whom I had followed for a long time before March 1952. Her systolic pressure varied from 200 to 240, and was occasionally 190; her diastolic pressure varied from 110 to 130. As in many reactive hypertensive patients, her anxiety was moderated during administration of plain phenobarbital. She had nervous tension, headache, vertigo, palpitation, exhaustion and depression. Then, in April 1954 the reserpine drugs became available. The only thing that bothers this woman now is her tendency to become fatigued. She is working as a teacher and as a seamstress in a department store, and she is probably one of the most grateful people you could have as a patient. This is due to treatment with reserpine alone.

Figure 2 shows the course of the blood pressure in a woman, aged 65, who had been on a maximum program of treatment, including digitalis and a salt-free diet. She saw a physician three times a week for mercurial injections and had had all of the other usual measures to rid the body of excess salt. Then the one missing factor was added, that is, effective treatment of her hypertension with reserpine and hydralazine. Previously, her pulse could never be controlled at less than 100. Digitalis and a low-salt diet were continued. After diuresis with mercurials, ammonium chloride could be stopped. This woman has now been maintained for more than two years with nothing additional but digitalis. We

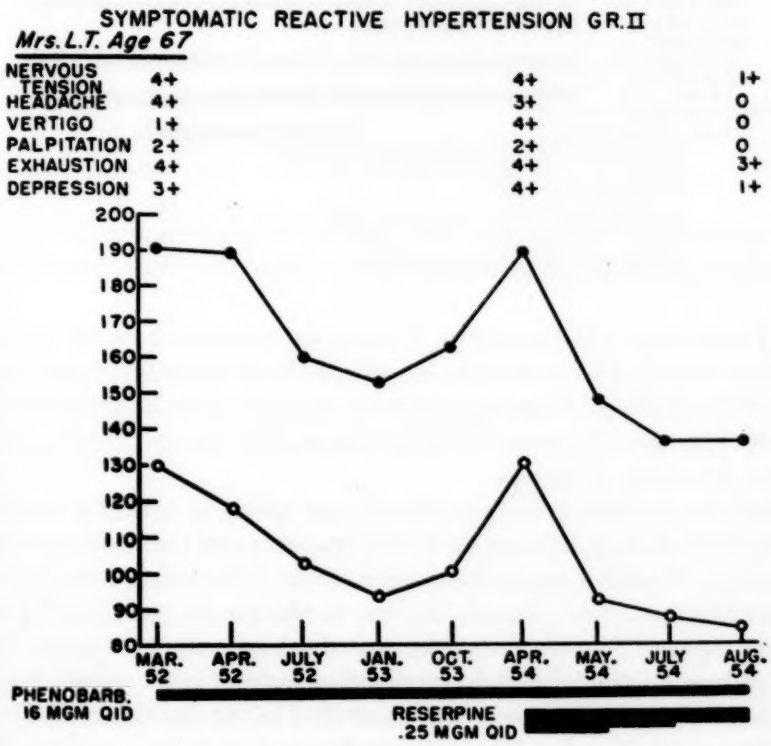

FIGURE 1

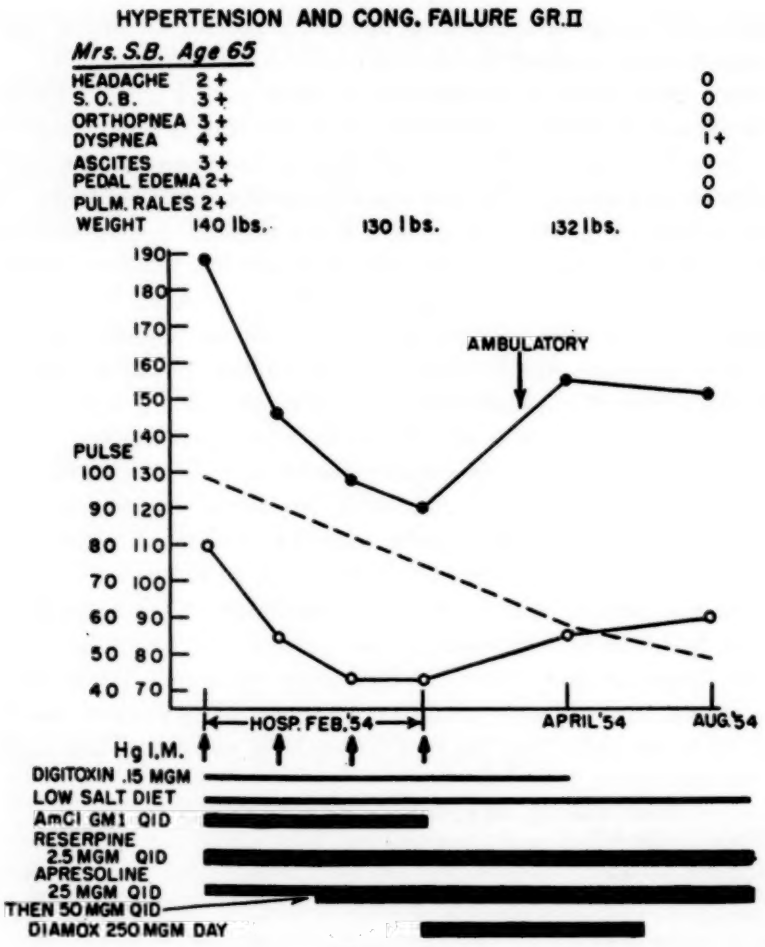

FIGURE 2

were able to liberalize her salt-free diet, and she is on a hypotensive regimen with reserpine and Apresoline in the dosages indicated on the chart. Diamox has been stopped.

Figure 3 represents the treatment of an acute emergency as far as congestive failure is concerned. This man was an elderly bank president who, during the winter of 1952–53 and the spring and early summer of 1953, had been hospitalized at least five times because of chronic congestive failure, chronic pulmonary edema, and disabling dyspnea.

I violated the general principles that I am going to tell you about in this instance by first starting Apresoline in this patient, and then rather shortly adding a ganglionic blocking agent (hexamethonium). There has been no reason to change this therapy, even though the use of the ganglionic blocking agent involves some danger. In this man, who was disabled with orthopnea, headache, shortness of breath, and intractable congestive failure, body weight was reduced to 207 pounds. The blood pressure was controlled in the vicinity of 160 to 170 systolic and 90 to 110 diastolic. He now runs his bank full time and has been able to take care of a quarter-acre garden plot.

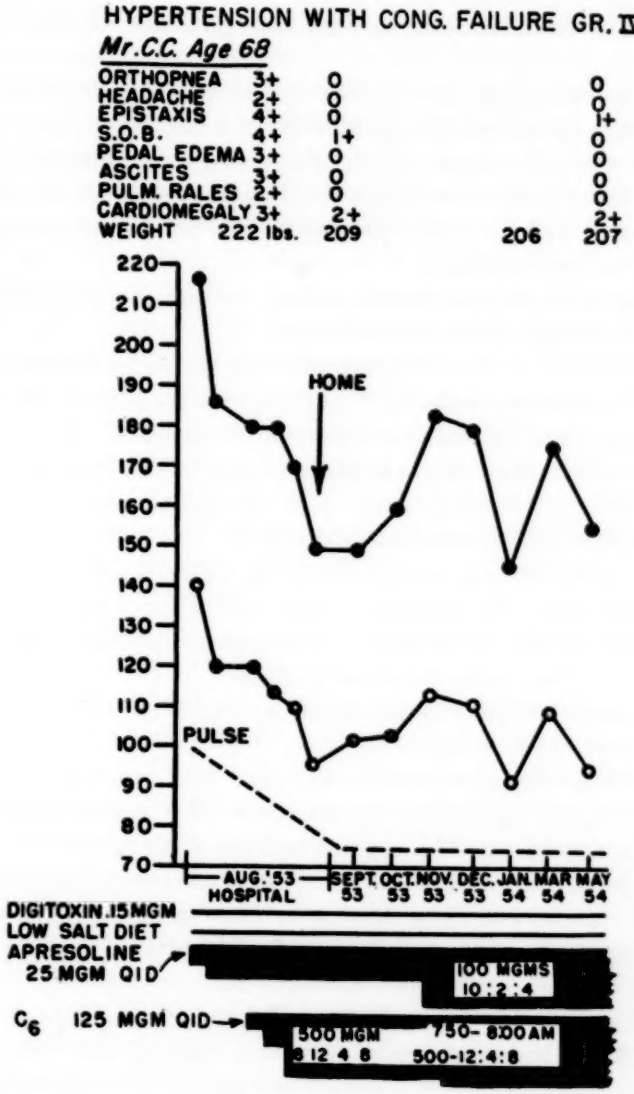

FIGURE 3

The scheme of treatment is the most important thing of all. The milder drugs should be tried before the more potent drugs are used. One should start with an average dosage of, for instance, 1 mg. per day of one of the refined reserpine drugs.

If this medication be given to 100 patients who are known to have had hypertension for a long time, 50 to 60 per cent of them will show an amazing drop in blood pressure, and they will be improved symptomatically. The reduction in blood pressure is highly beneficial.

Some patients will not respond to this treatment. You will have to use something more potent. The Veratrum drugs are not included here because I have not been particularly successful with them. A few of my patients have been benefited, but as a general rule the incidence of nausea and vomiting and other un-

pleasant digestive complaints is so high that patients will not take the medication.

Therefore, the next drug to add to the program is hydralazine (Apresoline). The initial dosage should be 25 mg. four times a day, and this treatment should be continued for about a week. Then, if necessary, the dosage should be raised to 50 mg. four times a day. I increase the dosage to as much as 600 mg. per day. That is as far as I will go with a patient who is not showing organic deterioration as a result of hypertension.

When dealing with organic deterioration, the ganglionic blocking drugs may be added in any dosage deemed necessary.

The last observation—and this is where I hope to be returned to fellowship with my panel members—is the fact that once the blood pressure is reduced, you will be amazed at what can be omitted from the program. Apparently, once you control whatever it is that causes hypertension, you can in many instances withdraw the ganglionic blocking drugs and, frequently, Apresoline or else maintain control with almost homeopathic dosages.

When ganglionic blocking agents are being used, caution should be exercised in removing them from the therapeutic program. If, in a patient who is adjusted to a normotensive level, the hypotensive regimen is suddenly omitted, a serious condition may develop, with pulmonary edema.

I shall let some of the other panel members challenge my position. I shall have a few more things to say later.

DR. LEVY: I want to correct one statement that was made. Dr. Gold and I were not referring to significant hypertension. We said systolic hypertension. What we really meant was the type of systolic hypertension that is unassociated with any particular symptoms—not hypertensive cardiovascular disease.

MODERATOR STONE: Dr. Lehr, have you some opinions on the use of antihypertensive drugs in the aged, and do you think that any of these drugs are contraindicated?

DR. LEHR: I should like to qualify Dr. Peltzer's statements.

There is a benign hypertension of the aged, that is, the systolic type with a normal diastolic blood pressure. I would say that in patients with this type, no treatment is required.

However, if the diastolic pressure is significantly elevated, nobody will deny that there is a condition which requires treatment. Even in such instances, in older people, the antihypertensive agents have to be selected with the condition of the patient in mind. An older patient with marked atherosclerosis has a much greater tendency to orthostatic hypotension than does a younger individual who has a better homeostatic mechanism, healthier blood vessel walls, and can adjust more readily.

Many authors think that ganglionic blocking agents should not be given to patients above the age of 60, except in emergencies like malignant renal hypertension. I would say that the thiocyanates also should not be used. I would give preference to the Veratrum alkaloids, because they do not have a tendency to induce orthostatic hypotension.

One should also consider, in treating hypertension in older people, that there are many complications that would not occur in the young adult, such as cerebrovascular accidents, myocardial infarcts, and peripheral thrombosis. These complications are due to the fact that, with the lowering of the blood pressure in patients with advanced atherosclerosis, the supply of blood to certain regions or organs may become inadequate. I am sure that some of you have encountered this type of complication or have read about it.

We should not make the mistake of concentrating treatment on only one almost physiologic sign of old age. I see no reason for lowering the systolic blood pressure if the only cause for its rise is the rigidity of the vascular system.

MODERATOR STONE: Thank you, Dr. Lehr.

DR. PELTZER: I would be the first to agree that one should not attempt to lower pure systolic hypertension. I thought I had covered that point when I opened my discussion. That condition isn't, in my mind, *significant* hypertension.

As regards the treatment of patients who are asymptomatic, in that they show no signs of organic deterioration, I think you have to evaluate the frequency of the complications that Dr. Lehr reviewed in terms of comparison with the frequency of similar complications from uncontrolled hypertension. That is the real source of controversy.

No statistics are available to help us determine whether we are doing real good or real harm, but I am sure that when congestive failure is part of the problem, lowering of the blood pressure will add a great deal to the efficacy and the simplicity of the program. The patient who is practically living on pills and a salt-free diet will be very grateful when you can liberalize his salt intake, once you have his hypertension under control.

MODERATOR STONE: Dr. Pardee, we have been discussing hypertension and atherosclerosis as important etiologic agents in heart disease of the aged, but irrespective of these factors, how does senescence itself affect the heart?

DR. PARDEE: It is difficult, of course, to determine in a given patient what is senescence and what is disease. But pathologists have a concept of senescence of heart tissue and of arterial tissue that we should bear in mind with regard to persons in this age group who have minimal symptoms.

The heart muscle itself becomes atrophied and degenerated. The fibrils and the nuclei do not have their normal appearance. The fibers, particularly, become smaller, so that there is a relative increase of interstitial tissue.

This situation is somewhat in contrast to that which results from chronic passive congestion or chronic anoxia caused by chronic coronary narrowing, and particularly to that in coronary occlusion, because in these conditions fibrosis is predominant. The difference is recognizable microscopically. In the case of infarction there are large areas of fibrosis.

Complete degeneration of the muscle fibers does not seem to be a part of the aging process.

In the arteries, also, there are changes which are attributed to senescence. The muscle does not degenerate to the extent that it does in the heart, but it

shows a decrease in the number of muscular fibrils and in the elastic tissue. Here also, there apparently is some increase in the fibrous tissue. There is also a tendency to lay down calcium in the deeper layers of the arterial wall. This does not seem to be preceded by the deposition of lipoid bodies. The aorta particularly is affected, and in the aged the aorta will show elongation and tortuosity, which result from degenerative processes and not from atherosclerotic processes.

Pathologists speak also of ectasia. I have had no personal experience with it, but it is said to be a form of extreme dilatation that occurs without much evidence of atherosclerosis.

The heart valves also sometimes show deposits of calcium, particularly in the annulus of the mitral valve. Calcium deposits also occur in the aortic valve itself.

The symptomatology that arises is difficult to separate from the symptomatology of the complicating diseases, that is, arteriosclerosis of the coronary arteries, hypertension, or some other condition; but there is an increasing tendency to shortness of breath. It usually does not reach a marked degree.

Occasionally, patients thought to have a considerable degree of heart failure have not shown evidence of coronary disease at necropsy.

Another common symptom is arrhythmia. It is thought that premature beats and auricular fibrillation particularly may occur without coronary disease because of senile changes.

The symptoms of the senile artery consist of tortuosity and increased pulsation of the arteries. There is an increase in the rate of pulse propagation, that is, the rate of movement of the pulse wave from the heart to the periphery. There is also an increase in the systolic pressure, which is probably not necessarily related to atherosclerosis.

There may be discomfort in the chest that arises on effort. One might think that this was due to coronary insufficiency, but it occurs in patients in whom you do not believe there is coronary disease.

These are the chief features of aging as it affects the heart. They are all similar to the milder symptoms associated with coronary arteriosclerosis. The question may be asked how far this degree of cardiac insufficiency can go when uncomplicated by arteriosclerosis. The question has not been answered, because the complication is so frequent, but many people believe that the insufficiency can progress to a considerable extent.

MODERATOR STONE: Thank you, Dr. Pardee.

Dr. Levy, I am going to ask you a broad general question with respect to the patient who has coronary artery disease in the later decades of life. What are your ideas about diet, work, exercise, smoking, and the use of alcohol?

DR. LEVY: These are all problems that have to be taken up with every elderly patient who has evidence of coronary atherosclerosis, with or without symptoms.

First, there is the question of diet. Any person who has attained the age of 70 let us say, in reasonably good health, probably has worked out a good scheme of living. It seems to me unfair and unnecessary, as a rule, to modify signifi-

cantly the dietary habits of such a patient with heart disease. Of course, if there is heart failure, we have to curtail the sodium intake; but I am speaking of the individual who is not in a state of failure.

For the most part, at present—and I say at present advisedly—we try to curtail the intake of total fats. It may well be, as we learn more about the intermediary metabolism of the lipid substances, that some other form of dietary modification will prove more effective.

Certainly, I think we have learned that mere curtailment of the cholesterol intake, such as telling people that they should not eat eggs, doesn't really make much difference; for it has been shown that the body can manufacture cholesterol from practically any type of food, whether it be fat, protein or carbohydrate.

To summarize, then, modify the dietary habits of the elderly individual with heart disease (or without) as little as possible. Eating is often one of the few pleasures left.

With regard to smoking, the same obtains. If a person with coronary heart disease has been an immoderate smoker, one is inclined to ask for moderation; but to insist that a man who has smoked for sixty-five or seventy years should stop completely, not only asks a great deal, but often takes away a solace and a means of stabilizing the emotions that may be very useful.

We all probably agree that a little alcohol is a good thing rather than the reverse. However, I have had patients say, "Well, I have never taken much alcohol. Do you think I have to take some every day?" The answer is "No, of course not." It is not really that beneficial as far as its effects on the vascular system are concerned.

The same principle applies, it seems to me, to the older patient as to the younger with respect to work. We know that many older persons carry on actively and well, and even improve, when they have some sort of job. People who are suddenly asked to give up what has been their life interest are unhappy individuals. Many of them are without avocations, and they don't do well.

Exercise, if prescribed, must be a suitable one for the particular patient—adjusted to his habits, his physical status, and his functional capacity. I have several patients over 80 years of age who have had minor coronary occlusions and who still play nine holes of golf with the aid of a golfmobile; they would be greatly upset if they could not do so. They enjoy it, and it does not seem to hurt them. Perhaps we can leave the discussion there.

MODERATOR STONE: Dr. Wilkinson, I should like you to discuss the general measures that are useful in the management of atherosclerosis and the things that are currently being done in an effort to throw some light on this subject.

DR. WILKINSON: I should like to re-emphasize that what we manage are the complications of atherosclerosis. This means that the patient has to have symptoms before we can know that the process has become complicated.

Many agents have been used in an attempt to lower the blood cholesterol level, to alter the cholesterol-phosphatide ratio, and to change certain concentrations of lipoprotein molecules or aggregates. The current stylish group of molecules are those with values between 20 and 300. That changes rather fre-

quently. Also attempts have been made to change the ratio of the alpha and beta lipoproteins.

There is no drug that I know of with which you can lower the blood cholesterol level to a significant degree, or change the alpha to beta lipoprotein ratio, or the negative Svedburg flotation units of lipoproteins, without certain effects that must be considered seriously before these drugs are used.

In our experience, choline and inositol are not effective. I think that has been borne out by a sufficient number of independent investigators, so that we can forget them as decholesterizing agents.

We have not been successful in the use of sitosterol or any of the vegetable phytosterols, a group closely related to cholesterol but of vegetable origin. Other physicians have reported good results or lowering of the blood cholesterol level. We have not been able to achieve this, and I believe that the consensus of physicians who have worked with sitosterol would be in agreement with our laboratory finding; the results obtained are difficult to interpret, and any changes are of such a degree that they are probably of no significance clinically even if they do appear mathematically significant.

The results of estrogen therapy are most impressive. We know that women before the menopause have a high serum alpha lipoprotein level as compared to beta lipoprotein, but this does not hold true after the menopause. Atherogenesis is much more prevalent after the menopause than before it. We know that a disease, like diabetes, that eliminates the sex difference in atherosclerosis is associated with an altered alpha/beta lipoprotein ratio. We can alter the ratio by the use of estrogen, but at present we have to geld a male to do so. In such a male, large breasts develop; he has loss of libido and, frequently, personality changes. In the opinion of many, these side-effects are far worse than the disease we are trying to treat. We must also bear in mind that the patient may have a disease process that has already stopped, or one that is in an irreversible stage.

At this time, the use of estrogen is still experimental. It is not yet a therapeutic weapon that we can use generally. We may develop it into something better in the future. Right now, we have no effective drug without serious side-effects that can change these various theoretically deleterious situations.

I should like to say that none of us knows whether or not a high blood cholesterol level is harmful. On the other hand, we won't know until we have been able to lower the blood cholesterol level effectively and to compare a group in which it has been lowered with a group in which it has not been lowered.

In regard to diet, the reduction of fat intake to less than 20 Gm. of extractable fat (and that is a little less fat than is in the rice diet usually prescribed) seems in some cases to lower the blood cholesterol level to a significant degree. Again, I mean "mathematically" significant. Dr. Kinsell, who is presiding here today, has been able to lower the blood cholesterol level by removing all animal fat from the diet and using long-chain unsaturated vegetable fats. This diet, again, is not one that I should like to eat for ten or fifteen years, nor should I

like to start at 25 years of age and eat this diet for the rest of my life with the idea of living an additional five or six years.

The situation now is that our choice is between going on a diet that a Spartan would not like, being gelded, or using drugs that have no effect.

MODERATOR STONE: Dr. Lehr, would you like to comment on this subject?

DR. LEHR: I am in full agreement with what Dr. Wilkinson had to say. At present, we have no drug that is really effective. However, I think that it might be advisable—and I am sure that Dr. Wilkinson will agree with me—to tell people as they grow older to restrict their total food intake, to keep their weight down, and to eat a fat-poor diet. I mean poor in animal as well as vegetable fats, although we have no definite evidence that that is helpful. I think we can say that, in general, lean people may have fewer coronary infarcts. Do you agree with that?

DR. WILKINSON: Not completely. I think that the idea of keeping the weight down is good. We use in our clinic a modification of the Metropolitan Life Insurance Company's tables. We use the weights as given up to 30 years of age and then allow the patients to weigh the same at 35; 5 per cent less at 40; 5 per cent less at 45; and 5 per cent less at 50, so that they actually reduce by approximately 13 per cent between 35 and 50 years of age.

The reason for this is that the average person becomes less active as he grows older, and what used to be muscle tissue is now adipose tissue. As regards telling older people to moderate their fat intake, we would be more likely to tell them to eat a fat-free breakfast. This is because the ability to remove fat from the blood stream after a fat load, seems to be decreased, and their behavior resembles modified familial hyperlipemia. In other words, the fat tolerance test shows a prolonged utilization curve. Rather than tell them to eliminate fats, we would tell them to have a fat-free breakfast and then to eat whatever they want for lunch and dinner. We adjust their weight as I have indicated.

MODERATOR STONE: Dr. Pardee, will you discuss for us, please, a question in two parts: First: What are the early manifestations and signs of coronary atherosclerosis? Second: Assuming that a patient has had a myocardial infarction as a result of atherosclerosis and has recovered, what is the rehabilitation program?

DR. PARDEE: The early stages of coronary arteriosclerosis are asymptomatic in many individuals. We all have seen symptomless patients with abnormal electrocardiograms of such character that we were certain that they were due to narrowing of the coronary artery.

The first symptoms that appear are of three kinds. The most common is the anginal syndrome in a mild form (perhaps as discomfort in the region of the lower sternum), which is relieved by belching and which comes when the patient walks or when there is an emotional reaction. This discomfort often is disregarded for a long time and attributed to indigestion, as you undoubtedly have observed many times.

The other common manifestation is an increased tendency to shortness of

breath upon somewhat more than ordinary effort. Here the possibility of the patient not being in good physical condition, or of having such pulmonary disease as emphysema or chronic bronchitis, must be considered. These things may cause a similar tendency to shortness of breath. This, and the anginal syndrome are the two most frequent symptoms.

The third is the development of cardiac arrhythmia. Sometimes this is in the form of premature beats, but most often it is in the form of paroxysmal auricular fibrillation. Fibrillation may occur in attacks which become more frequent with the progress of time, or it may be permanent from the beginning. This arrhythmia has already been mentioned as being one of the results of an aging myocardium. Its appearance at ages below 70 may be considered as probably due to coronary arteriosclerosis. Premature beats are less frequent but may be viewed in the same way. Heart block, however, must always be considered as due to coronary disease.

The earliest diagnostic physical signs are certain changes in the electrocardiogram. Sometimes these changes are not present if the electrocardiogram is taken while the patient is at rest, but they may be present if it is taken after strenuous physical exercise or after the inhalation of 10 per cent oxygen mixtures. Another sign that may be obtained, which is not conclusive but at least is suggestive of arteriosclerosis, is the roentgenographic appearance of the aortic arch. If the aortic arch shows increased dilatation, particularly with increased density, we may suspect that the coronary arteries also are involved.

The retinal arterioles do not furnish as good an indication of the condition of the coronary arteries. They belong to a different arterial system and are not affected by atheroma.

Sometimes a patient may have an attack of coronary thrombosis with infarction of the heart as a first manifestation of coronary arteriosclerosis. The question has been asked: What should be done to rehabilitate such a patient after the attack? It is important that rehabilitation begin during the attack. It makes the job afterwards much easier.

Many patients are alarmed by what they are told at the beginning of the attack—at a time when they are seriously ill. The doctor does not say much, and doesn't go into the details that the patient must know in order to understand the situation, and the patient is much disturbed by a flat diagnosis of coronary thrombosis. This may start mental reactions which will take months, or even years, to correct. Therefore, it is advisable to use care in choosing what to say to the patient during the first hours of his illness.

Physical rehabilitation begins shortly after the attack. We should let the patient move about in bed fairly soon, and let him sit up in bed much sooner and get out of bed sooner than has been the custom in the past. This should not be done routinely, but with consideration of the patient's physical strength, pulse, blood pressure and general appearance of well-being. Certain other things also must be taken into consideration, such as the duration of fever, the extent of the infarction as estimated from fall in blood pressure, the results of blood tests, and the character of the electrocardiographic changes.

It is very important to have told the patient the whole story by the time he

gets out of bed, namely, that he has had an attack, that he has made a good recovery and that his chances of having a serious recurrence, though unpredictable, are not as bad as they were thought to be a few years ago. The most recent figures show that of men having a first attack between 50 and 60 years of age, 65 per cent will live more than five years and 40 per cent more than ten years.

The patient must have this explained to him and he must be given an optimistic point of view. Physical rehabilitation should begin when he is allowed to get out of bed and to walk around. He should be told that it is perfectly all right for him to walk as soon as you think he is able to do so. The physician should not be overcautious and suppress the patient's activity for three months. Such a patient should return to work as soon as he is psychologically and physically ready. Both of these things have to be taken into consideration throughout the convalescence. No general rule can be laid down, because each step in rehabilitation must be guided by the severity of the patient's illness.

MODERATOR STONE: Dr. Gold, a matter of great importance comes up next. There is some thought that older people respond differently to digitalis, morphine and atropine than do young adults. Do you have some opinions on that point?

DR. GOLD: In general, older people are more sensitive to most drugs. That applies to the digitalis group, to quinidine, and to most of the sedatives, such as morphine. The response is the same qualitatively, but quantitatively it differs. It is important to bear in mind that less than the amount required by the young and the middle-aged will produce the same results in the elderly. If the doses used are the same as would be expected to produce the proper therapeutic effects in the younger age groups, they are likely to have toxic effects in the aged.

MODERATOR STONE: We have received a large number of questions from the audience. In order to try to cover the points in which you are interested, I shall allow the panel members to take five minutes each to answer the questions that have been directed to them.

Dr. Peltzer, will you take yours first.

DR. PELTZER: The first question pertains to sensitivity to reserpine and to drugs that may be used in place of it.

The only contraindication to the use of reserpine, in my mind, is the development of depression or parkinsonism, which occurs only rarely. Most of the other side-effects of reserpine are, at most, bothersome. A patient's nose may become congested, but nose drops instilled at night will ordinarily give relief. One pharmaceutical house markets reserpine together with pyrrobutamine (Pyronil), which is helpful in providing relief. I rarely recall ever having had to stop the medication because of the nasal congestion becoming so severe that it could not be controlled.

Actually, when reserpine is used, some of the side-effects of the drug are helpful. I mention the effect on the mood because elderly patients with hypertension, particularly, are apprehensive and anxious and concerned about their condition—if it has been revealed to them, which is usually the case. One is very grateful for the mood-moderating effect of reserpine.

Reserpine is effective in masking the side-effects of some of the other drugs

being used. With Apresoline, headaches, dizziness, nausea, anorexia, and vomiting may be so frequent that the drug cannot be continued. However, when it is administered in addition to a basic program of reserpine, the response is satisfactory.

The next question is: Given a patient with angina induced by effort, how militantly should his hypertension be combatted?

That is an interesting question, because, rather recently, at least one investigator found that when he used reserpine he obtained a gratifying decrease in the frequency with which nitroglycerin was necessary. He advocates reserpine for angina pectoris.

I would not be afraid to give reserpine to a patient with angina in dosages up to 2 mg. a day, if I found it necessary to control his hypertension. However, if it is necessary to use Apresoline, you must remember that this drug increases cardiac output. With a fixed coronary artery system, increasing the patient's cardiac output with Apresoline may well induce angina and even disaster. Apresoline may be used if necessary, but it must be administered cautiously. If I found it necessary to use hexamethonium, I would be extremely cautious.

The next question is: Is there any danger of increased angina as the blood pressure falls?

That is theoretically possible and probably does occur occasionally, but relief from angina occurs more frequently than an increase in angina.

One more question: Do you believe that if a patient is permitted to remain in a state of hypertension, complications will soon develop?

The whole point of my effort here this afternoon is that if hypertension is not controlled, we have no way of knowing who is going to have a myocardial infarction or who is going to have a cerebrovascular accident. Every year some patients with hypertension will get into difficulty. Therefore, the point of my thesis is that even in those who show no organic heart disease, corrective measures may be used to a certain reasonable extent. That reasonable extent ends, in my mind, with the use of reserpine and Apresoline. I would not use the ganglionic blocking drugs in a patient who showed no significant organic deterioration as a result of blood pressure elevation.

MODERATOR STONE: Dr. Levy, will you answer your questions now, please?

DR. LEVY: There is one question that I shall discuss briefly: The use of Dicumarol in aged individuals with coronary occlusion or thrombosis.

It has already been pointed out that older people react with greater sensitivity to drugs than do those in the younger age groups. This obtains with respect to the anticoagulants. An older person—let us say one over 65 years of age—who has a cardiac infarct is likely to be less sick and to have a smaller area of involvement than a younger individual, because his atherosclerosis has been developing over the years and there has been opportunity for the formation of a collateral circulation.

Theoretically, if we believe in anticoagulants, every patient should be given the benefits of their use. On the other hand, some physicians do not use them at all, because they believe that the statistical evidence is inconclusive and that

the dangers accompanying the use of anticoagulant drugs are still considerable.

In general, unless an aged patient showed evidence of a considerable area of involvement, I would be willing to risk omitting anticoagulant therapy.

There are several questions on the use of radioactive iodine. In a few selected patients with intractable failure, or in patients with intractable anginal pains—and there are, I may add, relatively few—radioactive iodine judiciously given has apparently helped. Our experience with it, for the most part, has been in patients with congestive failure rather than in patients with pain, and we have seen favorable effects in several instances. The experience in Boston has been more extensive, and the enthusiasm of the workers there is somewhat more intense than ours. They have reported up to 70 per cent improvement. Perhaps our results with radioactive iodine are not as good, because we have used it only in the more advanced cases. It is worth a trial when other measures have failed and it is safe if cautiously employed, that is, given in fractional doses at intervals rather than in a large dose initially.

I shall answer only one more question: What techniques are available to the practitioner for evaluating the functional capacity of the heart?

We have no test that will measure that physiologic function. We make an estimate based largely on the patient's history and on his response to effort, to everyday exertions, or to the more unusual ones that he may attempt. There is no technique available at present which will express cardiac function in numerical terms.

MODERATOR STONE: Dr. Gold, will you please discuss your questions.

DR. GOLD: I have the question: Will you discuss the prevention of coronary heart disease for a middle-aged person?

I presume that the questioner has in mind a middle-aged person who thinks he is normal and has no evidence of heart disease. What should he do about his life in order to gain some assurance against the development of coronary heart disease?

We have already had some suggestions. I should mention immediately that we do not know for certain the answer to that question, but we do have suggestions that emerge from general experience, theoretical thinking, and experimental work. There is the point, which Dr. Wilkinson and Dr. Lehr discussed, about diet and the control of the blood cholesterol level. The indication seems to be that coronary heart disease is less apt to develop if the weight is kept down and the total fat intake reduced. Keeping the weight down by the systematic control of diet is particularly applicable to the individual with an inclination toward gain in weight.

I know of no medicines that we can even suspect of preventing coronary heart disease. One phase of this condition, acute coronary thrombosis, develops in the person who already has some coronary heart disease. A separate question can be asked: Is there anything that a man in middle life, who knows that he has coronary disease but who has not had thrombosis, can do to prevent an acute episode that leaves him temporarily unconscious and perhaps incapacitates him?

In the matter of prevention, physicians in general have emphasized the limi-

tation of physical activities. That brings up the question of retirement. Should the patient retire from his job?

I should like to offer a general answer. One of the major factors accounting for the precipitation of an acute attack of coronary thrombosis in an individual with coronary heart disease is the emotional state. The problem becomes one of controlling anger, hate and aggression in the middle-aged person with coronary heart disease. How do we know that? We have no comparative statistics, in relation to coronary thrombosis, on what happens to people who do and do not become angered easily, but we do have the general experience that in relation to a sudden violent emotion or rage, patients have died suddenly or have had an attack of coronary thrombosis. If that is the general experience—and I believe it is—it seems that if we can control the emotions, we shall to that extent be able to reduce the chance of acute coronary thrombosis.

A shifting of emphasis from limitation of the physical activities to control of the emotions is necessary. We do not accomplish this by sedation, but we do achieve moderate success by appropriate talks with the patient. Let him express his emotions freely until you can point out to him what he is doing—that in his endeavor to kill someone else, he is accomplishing the opposite, that is, killing himself. It is difficult for a patient to realize this, but if the physician's attention is directed to pointing it out, there will come a time when the status of some of these patients will improve.

I have another question: What is your opinion of potassium iodide as an adjunct in the management of hypertension?

I think it has no particular value in hypertension. It was introduced in the treatment of arteriosclerosis because of a mistaken notion. This notion arose from the observation that iodides tend to reverse the precipitation of proteins in the test tube. It was introduced into the therapy of syphilis in order to liquefy the gumma. I don't know if it ever did liquefy the gumma, but it was extended to the treatment of arteriosclerosis in an endeavor to rectify the misbehavior of the proteins in the cell. Potassium iodide may have some value in arteriosclerotic patients who have changes of that sort. I think the patients feel better when they take it. But then, we must remember that patients feel better with anything they take if it is given in just the right way.

Here is another question: Should digitalis be given at the same time as quinidine to a patient with myocardial infarction, flutter, or failure?

They are frequently given at the same time. I have given them concurrently in various situations, but prefer not to, and avoid doing so whenever possible. My reason is not based on observations in human beings, because good statistical information cannot be obtained in that way, but is based upon pharmacologic experiments. In a heavily digitalized dog, for example, small doses of quinidine which by themselves induce no disturbance in heart rhythm, can cause bizarre disturbances in rhythm, complete ventricular standstill, and attacks of ventricular tachycardia. In certain combinations, these two drugs apparently cause unpredictable disorders of cardiac rhythm. Since that effect is established as true for animals, there is no reason to believe that it may not occasionally account

for one of the disastrous results that occur when either or both of these drugs are in use.

Is there any need for a drug with similar action but less toxicity than digitalis?

The answer is, "Yes, there is." Who wouldn't like a drug that causes just as much therapeutic effect, with no toxic effect? I fear that such a combination is unlikely. Apparently it is impossible to have digitalis action without digitalis toxicity. The indications are that toxicity is much the same for all the digitalis preparations now available.

MODERATOR STONE: Thank you, Dr. Gold.

Dr. Pardee, will you take your questions now.

DR. PARDEE: Are any of the arrhythmias of the aged attributable to a disturbance in thyroid activity? If so, with what frequency?

The thyroid is a cause of arrhythmias in the aged, but not often. Arrhythmias usually occur as a result of anoxia or lack of circulation in certain focal areas in the myocardium, due to coronary arterial narrowing. Hyperthyroid states in the aged occur especially in association with small tumors, which may not be palpable or easily demonstrated. The physician must watch for this. However, it is a comparatively rare occurrence.

The other two questions are about the electrocardiogram. The term "routine electrocardiogram" is used in each case. The questions are: Should a patient eat before the routine electrocardiogram? Should a patient smoke before the routine electrocardiogram?

The answer to both is, "Certainly not." When we take a routine electrocardiogram, we are attempting either to obtain a basal state for control in order to judge future changes that may occur in the electrocardiogram, or to appraise the state of the myocardium uninfluenced by drugs or the particular nervous influences which apparently arise as a result of digestion.

In certain patients who have mild coronary disease, eating a meal can give rise to the changes in the electrocardiogram that we attribute to coronary insufficiency—similar to those produced by a moderate amount of exercise. Smoking, in addition to having a possible vasoconstrictor effect upon the arteries, causes an acceleration of the heart rate and a rise in the blood pressure. There may be a specific drug effect upon the myocardium. We know that some people show a surprising change in the electrocardiogram as a result of smoking one or two cigarettes. The percentage of such people is not inconsiderable.

Patients should never be allowed to eat or smoke before a routine electrocardiogram. The record would not be comparable with one taken later without prior smoking or eating.

MODERATOR STONE: Thank you, Dr. Pardee. Dr. Wilkinson, I shall call on you.

DR. WILKINSON: The question is: What is your position regarding the atherogenic index of Gofman? Is there any procedure that enables one to diagnose atherosclerosis in an individual by means of an electrocardiogram?

A term I shall have to use here is "random prediction." If you take a hundred marbles, half of them red and half of them white, put them in a box, blindly select a marble, and say yes or no, depending upon whether it is red or white,

that is random prediction. Prediction based on atherogenic index, total cholesterol level or the cholesterol/phospholipid ratio is approximately 10 per cent better than random prediction. That means that if a patient is sitting across the desk from you, and you use results of these three tests as a basis, your prediction regarding the possible development of clinical complications of atherosclerosis will be about 10 per cent better than random prediction.

When based on the alpha/beta lipoprotein ratio in patients below the age of 35 or 40 years, however, the prediction is about 35 per cent better than random prediction. It is obvious that there is no test in the range of sensitivity of the Wassermann reaction.

We believe that a patient with clinical angina pectoris can be presumed to have coronary atherosclerosis. In necropsy studies, this is borne out in approximately 95 per cent of the cases. Therefore, even if a person with clinical angina pectoris has a normal electrocardiogram, we assume that he has coronary atherosclerosis.

The next question is in reference to intensive lipotropic therapy in the treatment of cardiac involvement: Are lipotropic agents important as prophylactic measures?

I mentioned earlier that we have not been successful with them. Their use probably has been based on a misconception. The fatty liver that is a result of a choline-deficient or methionine-deficient diet is helped by administration of choline or methionine. That has nothing to do with the fat between the intima and the media of the arteries; we are not sure this is the result of a diet deficient in choline or methionine. Atherosclerosis can be induced in experimental animals by varying the proteins in the diet, but time is too short to discuss this matter.

Is cholesterol still regarded as a factor in atherosclerosis? Isn't it true that the original work on cholesterol was carried out on rabbits and has since been discarded as of no value since rabbits are herbivorous animals?

Even a further comparison can be made. If you were to eat the amount of natural foodstuffs containing the equivalent of the amount of cholesterol that is added to a rabbit's diet per kilogram to induce atherosclerosis, you would consume per day approximately 2 kilograms of yellow cheese, 15 whole eggs, 10 liters of whole milk, 1 kilogram of butter, and 4 kilograms of lean beef.

Have the effects of combined androgen-estrogen treatment been tried?

They have. Investigators who have tried to avoid the feminizing effects of estrogen therapy by adding androgens found that, when the feminizing effects were lacking, there was a reversal of the alpha/beta lipoprotein ratio from the "debutante" to the "old goat" pattern.

MODERATOR STONE: Dr. Lehr.

DR. LEHR: The first question concerns the use of digoxin, digilanide C (Cedilanid), and digitoxin as compared with *Digitalis lanata*.

Digoxin is obtained from Cedilanid (lanatoside C) by hydrolytic cleavage. On a weight basis, digoxin is about twice as potent as Cedilanid. Digitoxin is one of three glycosides contained in both *Digitalis lanata* and *purpurea*. It is the most

powerful, best absorbed, and most toxic principle among the digitalis glycosides. Its use requires caution and careful supervision. It should not be employed routinely by the general practitioner, particularly in the treatment of older patients who are more sensitive to digitalis, and therefore may more readily show signs of digitalis intoxication.

Digitalis lanata is a species of digitalis that contains the three glycosides digilanide A, B and C (digilanide or lanatoside C is known commercially as Cedilanid.) Upon hydrolytic cleavage one obtains from these digitoxin, gitoxin and digoxin. One commercial preparation contains all three glycosides in purified form (Digilanid).

I think the most important point to remember in connection with the use of digitalis preparations is that treatment with this drug is an art; it has to be individualized more than any other type of therapy, and the patient must be carefully watched for signs of overdosage. The long-term experience of a physician with one particular digitalis preparation may outweigh the advantages to be gained by switching to a more "modern" and more purified glycoside.

The second question is: Will you express an opinion on the applicability of intravenous adrenocortical steroids in shock due to myocardial infarction?

I think that shock in myocardial infarction is mainly due to dysfunction of the myocardium. In such cases, if the blood pressure drops to the dangerous level of 70 or below, one can try intravenous drip infusion of arterenol. Another measure that has been suggested, particularly in Europe, is the administration of small repeated doses of strophanthin preparations intravenously. The object is to maintain blood pressure at a level that is consistent with adequate body functions, realizing that this therapy in itself is not without danger.

If one is thinking of the stress connected with myocardial infarction, and a deficiency of adrenocortical function is suspected, then possibly cautious administration of adrenocortical hormones may be justified.

MODERATOR STONE: Dr. Kinsell, that completes the panel to which we were assigned.

CHAIRMAN KINSELL: Dr. Stone, in behalf of all of us who have listened to you, I should like to thank you and the panelists for a beautiful job.

One last word. I heartily agree with Dr. Wilkinson in that I should dislike extremely to try to eat long-chain unsaturated fats as the main article of diet for the rest of my life, or even for a small portion of it.

However, I suggest to Dr. Lehr that we should all, perhaps, think of individualizing fats rather than grouping them together, because there are vast differences in saturated and unsaturated fats. What this means in relation to atherosclerosis, no one knows; but there is a difference as between day and night, in so far as the effect upon plasmolipids is concerned. I would suggest also that, since a great portion of ingested carbohydrate is changed to fat which happens to be saturated fat, the general emphasis should be much more upon limitation of calories than upon limitation of fat.

THE SURGEON AND THE ANESTHESIOLOGIST AS A TEAM FOR GERIATRIC SURGERY*

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The surgical team, like other teams, exists for the purpose of achieving a specific goal by combined efforts. The surgeon and the anesthesiolgist are interdependent, as extensive surgery cannot be performed without a means of providing relief from pain. The need for anesthesia would not exist without a patient undergoing surgery.

Modern surgery has become more complicated by being extended to areas of the body that are vital, and therefore a combination of special skills must be used in order to accomplish the desired goal.

The surgeon's efforts must be utilized without interruption of the delicate operation he is performing. The anesthesiologist must be the clinical physiologist and pharmacologist whose skills are used to maintain respiration, circulation, and the metabolic homeostasis of the organism.

Smooth operation of the surgical team arises from mutual confidence between the surgeon and the anesthesiologist. The surgeon who must be constantly concerned with the patient's respiration and circulation cannot fully devote himself to the task of operating. The anesthesiologist, in like manner, cannot function properly if he fears that his warnings of danger will go unheeded by the surgeon. As with any team, there must be a chief, and the surgeon rightly has that function at the operating table. However, he must delegate certain responsibilities to the competent anesthesiologist who is working with him.

The morbidity and likelihood of mortality of the surgical patient will be reduced by the close cooperation of the surgeon and the anesthesiologist as a team. The surgeon who attempts to control, without consultation, all phases of an operative procedure is not availing himself of the modern advances in surgical teamwork.

The elderly patient presents a challenge to the surgical team through the very nature of the physical deterioration that is associated with the aging process in all tissues of the body. However, the chronologic age of the patient may be entirely different from the physiologic age of his tissues and systems. Many of our patients in the older age groups chronologically, may be young physiologically. The majority in older age groups have defects primarily in the pulmonary and circulatory systems. Thus, at the outset, the surgical team must deal

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with a patient whose response to trauma is slower than in a younger person and frequently is inadequate to cope with the stresses of the operation.

MANAGEMENT

Physical status

Emphysema is the great destroyer of normal pulmonary function in the older age group. This condition diminishes ventilation and causes deficits in respiratory gas exchange. Through the administration of anesthetics and of drugs which depress respiration, the patient is easily placed in a situation in which hypoxia and hypercapnia are readily induced.

The aging process is associated with increased rigidity of the circulatory system. The peripheral vascular bed can no longer respond quickly and adequately to changes in its environment.

The cardiac muscle frequently has been partially replaced by fibrous tissue. The coronary vessels no longer have the pliability of youth. The patient makes a poor adjustment to sudden blood loss, extreme positions on the operating table, and deep anesthesia. Thus, it becomes obvious that the older patient has a narrow margin of safety, and a narrower margin for which he can compensate to maintain homeostasis. The elderly patient, then, is an ideal subject in whom to demonstrate the value of the smoothly performing surgical team.

A careful evaluation of the physical status and the operative risk of every patient undergoing surgery is mandatory. This is especially true in the older age group, for pre-existing disease may make the management of anesthesia extremely difficult.

A careful history and physical examination are essential for the evaluation of these patients. All necessary consultations should be procured well in advance of the day for operation, so that an accurate appraisal can be made. Elective surgery should not be undertaken lightly. A complete blood count and urinalysis are mandatory, and all other laboratory data should be available before the planned operation is begun. We hesitate to make a routine procedure of any one test. However, a chest plate and an electrocardiogram may furnish some previously unsuspected important data. If suspicion has been cast upon a specific organ or system, additional data should be available well before the day of contemplated operation.

Premedication

The elderly patient approaching surgery may be anxious, as may be a patient at any age. Some form of sedation should be ordered an hour or two before the scheduled beginning of the anesthesia. For many years, opiates or belladonna derivatives have been given for this purpose. However, because of recent knowledge that the beneficial nature of the opiates when used for premedication is far outweighed by the resulting damage to respiration and circulation, we do not use them. An appropriate dose of a barbiturate will provide the necessary sedation without the crippling effects of opiates on the circulation and respiration. This change in premedication has eliminated a severe and unnecessary stress which once was placed on the geriatric patient.

In patients of extreme age, atropine alone may be the only premedication necessary. Scopolamine is not a wise choice in this age group, as the patients may become irrational and difficult to manage.

Anesthesia

The choice of anesthetic agent and technique will depend primarily upon the anesthesiologist. However, in this age group deep planes of anesthesia are, in general, disastrous. The lighter the plane of anesthesia that can be maintained compatible with the surgical requirements of the operation, the more salutary is the situation for the patient, regardless of the anesthetic agent used. Unfortunately, it is true that every agent in use today for general anesthesia decreases cardiac output, and the more profound the anesthesia the greater the decrease. The decrease in cardiac output is the result of depression of the myocardium and dilatation of the peripheral vascular bed. Light anesthesia minimizes this fall in output, and thus elderly patients may undergo surgery and anesthesia without mishap under light planes of anesthesia.

The anesthetic technique will vary with the operative procedure. These patients usually have varying degrees of emphysema; thus, assisted or controlled ventilation is mandatory for adequate oxygenation. It is most important that carbon dioxide be removed from the alveoli.

Operation

The operation itself introduces problems because of the lack of respiratory and circulatory compensation in patients in the older age group. The position on the operating table is very important. It must be compatible with the physiologic tolerance of the patient. All routine positions for any operation must be modified so that the patient will tolerate the stress. The extreme Trendelenburg, the kidney position, the lateral position, and the extreme lithotomy position invite circulatory or respiratory embarrassment. Careful attention must be given to modification of these positions as soon as it becomes apparent that the patient will not tolerate one of them. A fall in blood pressure, or tachycardia may be early indications that the stress of position is excessive for the patient and that modification is mandatory.

The duration of the surgical procedure assumes greater importance in the old age group. It is difficult to say what is meant by a long operation in these patients, but the procedure and repair must be accomplished as quickly as possible and without unnecessary delays. Elderly patients tolerate one-hour to three-hour procedures extremely well, but when the operation lasts from four to six hours, deterioration of the patient becomes apparent despite the best management.

There may be an indication for an operation performed in stages, or for a compromise procedure that will protect the patient from the ill effects of the condition for which the operation is undertaken without exceeding his capacity to withstand surgery. For example, an elderly patient with acute cholecystitis

and borderline cardiac compensation due to arteriosclerotic heart disease may withstand a simple cholecystostomy well and be in better condition to have a cholecystectomy months later, whereas the latter procedure might be followed by death if it were performed during the acute phase. Physiologic tolerance has a meaning not only for the position on the operating table but also for the duration of the operation.

Patients of advanced age can withstand a moderate amount of trauma, but gentleness in manipulating tissue and organs is desirable. Roughness produces reflex activity that may be poorly tolerated and may add many complications to the postoperative course. If the surgeon is gentle, a much lighter degree of anesthesia may be maintained. On the other hand, if the surgeon is rough, the anesthesia must be deeper in order to obtund disturbing respiratory or cardiac reflex activity.

In this age group, signs of impending circulatory dysfunction must be recognized early and the operation stopped immediately for evaluation of the situation. A condition that may result in morbidity and fatality, if allowed to progress, can usually be prevented by early recognition and prompt treatment. The surgical team must stop immediately and consult quickly.

Ventilation during the operative course is perhaps the most important single factor requiring control during anesthesia. Since the geriatric patient undergoing surgery frequently has a respiratory defect, adequate and vigorous respiration must be maintained, both in depth and in rate, in order to prevent respiratory acidosis. Inadequate ventilation may result in an electrolyte imbalance that may be difficult or impossible to correct in the postoperative period. The accomplishment of adequate ventilation will vary from individual to individual, but it must be the primary concern of the anesthesiologist.

Careful attention to blood replacement is obviously necessary. In the geriatric patient with a chronic illness, the possibility of chronic shock must always be kept in mind; an early drop in blood pressure during an otherwise uneventful surgical procedure may warn of a decrease in blood volume. Therefore, blood volume determinations assume greater importance in this age group, in order to rule out the possibility of chronic shock prior to surgery and initiation of anesthesia.

Postoperative period

Postoperatively, the problem of pain is ever present. Too vigorous treatment of pain with opiates in patients in the older age group courts disaster. Large doses of opiates ordered routinely—in an effort to be kind to the patient—may cause a fatality following an excellent surgical procedure. The doses of analgesics should be minimal. It is preferable to permit minimal pain than to treat pain too vigorously. A small amount of pain keeps these patients moving well, which is most important in the postoperative period; and yet the pain should not be so severe as to limit ventilation. To a surprising extent, analgesia can be obtained with codeine in patients in this age group, without the profound effects on circulation and respiration which follow the use of potent opiates.

During the past eight years, we have kept a careful record of pulmonary complications following surgical procedures in all age groups. We believe that their incidence is indicative of the results to be obtained by close cooperation between anesthesiologist and surgeon. Although the data have not been divided by age groups, we observed that the morbidity from postoperative complications of all types (including pulmonary) is definitely if only slightly more frequent in patients 65 years of age and over.

We found that the incidence of pulmonary complications following surgical procedures decreased from 1.0 per cent in 1947 to 0.22 per cent in 1954. The incidence of pulmonary complications related to anesthesia was reduced from a high of 80 per cent to a low of approximately 20 per cent and during the last four years we have had no fatalities from this cause. This decrease in pulmonary complications mirrors the overall decrease in morbidity and mortality.

CONCLUSIONS

The elderly patient withstands surgical procedures well. Every facet of the operation should be carried out with a minimum of stress. One stress or insult, whether from surgery or from anesthesia, inflicted on a patient in this age group may initiate a train of events that will lead to death. If multiple stresses are allowed to occur, such as an extreme operative position, a prolonged operation, and inadequate pulmonary ventilation, morbidity or fatality will result. However, if careful attention be paid to detail, and each member of the surgical team does his share to prevent stress, the geriatric patient will fare well in the hands of the surgeon and anesthesiologist working as an operative team.

COMMON DIAGNOSTIC HAZARDS IN THE ELDERLY

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Physicians with care of the elderly are well aware that many disorders benefit more by treatment at home than by admission to the hospital. In many areas of Britain, the visiting by a geriatrician of patients whose family doctors have requested admission to the hospital originated in order to assess the severity of the case and so to arrange the priority of admission. This was essential, since most newly-formed geriatric units inherited huge waiting lists from the old chronic hospitals and institutions which existed prior to 1948, and it was urgently necessary to reduce these lists to practical proportions. As we visited these patients it became clear that a geriatrician could use his visit more profitably than merely assessing for admission to the hospital. Some patients dreaded our visit because they did not wish to go to a hospital; some asked how they could be helped at home; many did not know that their admission had been requested, as their doctors neglected to tell them or, from various motives, their relatives had tried to have them "put into hospital." The belief that a patient can be sent into a hospital regardless of his wishes is widely held by doctors and laymen. We may advise but never order.

Thus of the 574 female patients whom I visited in 1955, 270 were subsequently admitted to the geriatric unit. What of the other 304? If we decide against admission then we must offer some alternative plan to help the family doctor and his patient, and the prerequisite of any rational management is accurate diagnosis of the patient's illness or disability. I believe one can achieve a greater accuracy in clinical diagnosis by a leisurely examination of an elderly person in his own home with relatives or a friend present than having him brought, apprehensively, to the formal out-patient clinic; therefore, I now see all new patients in their homes. An almoner always accompanies me; the visits are always made in daylight to lessen the chances of a mis-diagnosis, but this means that the family doctor can seldom be present. He leaves a note of his opinion which is attached to my notes and filed with them. A rough analysis of these opinions places 90 per cent of the elderly in one of five generic categories, without differentiation. This is not an unusual practice and has been reported by Zeman (1). It is proposed to discuss some hazards of bedside diagnosis within these groups.

SENILITY

Senility is a word to be avoided. It means old age, which is not a disease. It lacks clinical significance. However, a geriatrician must try to understand what others may mean by senility, and perhaps there is evidence of progress in geriatric medicine in that the term now appears to be restricted to those conditions

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in which mental change predominates instead of to almost every condition, physical and mental, occurring over the age of 65!

So when asked to see a "senile" patient I am usually confronted by one over 75 who has an intermittent confusional state of long duration, is unable adequately to care for herself, is a nuisance to her relatives and neighbours, and has habits embarrassing to all bar the patient.

The common hazards are:

1. In mild cases, a failure to recognize the normal mental changes accompanying old age. If such patients are inadvertently admitted to the hospital the result may be disastrous, since mental adjustment to age can only be carried out in their normal environment. There is no virtue in training a person to live permanently in a hospital.

2. Failure to distinguish the common psychosis due to cerebral arteriosclerosis whether focal or diffuse, from that rarer one due to global cellular atrophy, commonly called senile psychosis. The confirmation of arteriosclerotic psychosis rests upon physical grounds. Careful examination of the central nervous system will reveal significant evidence, depending upon the brain areas damaged or upon release signs therefrom. This contrasts with senile psychosis, in which the central nervous system appears intact clinically. Kay and Roth (2), in an excellent article, have stressed an important sex difference between female and male senile psychotics, *viz.*, many women are in good physical health and may survive under care for many years, whereas most men are more generally enfeebled and have a high mortality. Since recovery to enable the patient to live outside a hospital occurs in arteriosclerotic psychosis, but never with senile psychosis, the practical value of differentiation is obvious.

3. Failure to suspect an organic dementia of nonvascular origin, *i.e.*, a psychotic disturbance due to organic disease. Common causes are primary and secondary intracranial tumors, chronic alcoholism, general paresis of the insane, severe vitamin B deficiency and chronic anoxia of any origin. A reasonable physical examination will usually afford evidence of the primary disease.

4. Failure to recognize a subdural haemorrhage (haematoma). This is tragedy indeed, since at almost any age it is possible to wash out the clot and dramatic recovery follows.

5. Failure to recognize that many drugs cause a confusional state—some with great ease in the elderly. The time-honoured one was bromide, seldom now prescribed, but still an ingredient of some patent medicines. Within the past year I have seen examples of confusion which have responded dramatically by stopping such varied drugs as trihexyphenidyl (Artane), insulin when used without blood-sugar estimation, barbiturates aggravating the confusion they were used to suppress, chlorpromazine, and many hypotensive agents.

6. Failure to recognize that the confusional state may not be confusion but a true depressive psychosis. These patients have no place in the geriatric wards, but must be placed under skilled psychiatric care, as they constitute suicide risks and may improve dramatically with electroconvulsive therapy.

ARTHRITIS

I have commented elsewhere (3) upon the unfortunate belief of so many elderly that painful arthritis is to be expected in old age, with the result that they may long delay seeking advice. Broadly speaking, if a patient of any age has signs and symptoms of one of the arthritides, but is capable of attending an out-patient clinic, then his family doctor will refer him either to a general physician with an interest in rheumatic disorders, or to an orthopaedic surgeon, or to a specialist in physical medicine. When the geriatrician is called out, he will see a bed-fast or room-fast cripple, who either has not sought advice until this late stage, or who has had a relapse after benefiting from earlier treatment.

If domiciliary examination confirms the diagnosis of arthritis, then admission for further assessment, and for initiation of treatment is desirable. Radiology will assist in establishing the type of arthritis, but should not of itself determine treatment. It is not uncommon for both hip joints to show osteoarthritic changes. On the other hand, the worst joint radiologically may have no symptoms; yet its fellow, less affected radiologically, may be crippling the patient. Again, a common and unexpected finding may be Paget's disease of bone. Is it contributing to the symptoms? If so, treatment with combined androgen and estrogen may bring relief when other measures fail. Symptomless localised Paget's disease should be observed, untreated, since it may never trouble the patient at all.

But what can mimic arthritis? There are three major hazards.

1. Some degree of degenerative change in joints is part of the normal aging process. There may be clinical evidence of degenerative arthritis in knees or hips, but the vital point is to establish whether such changes account for all the patient's symptoms and signs. I am frequently asked to see patients who are house-borne due to frequent falls, as their "arthritic knees let them down." A careful history and full examination is more likely to reveal an unstable cerebrovascular system than an unstable knee.

2. When stiffness around the joints is associated with difficulty in getting about, it is necessary to exclude early Parkinson's disease. Frequently it is this condition which is the undetected factor in patients not responding to treatment of arthritis. Garland (4) has stressed that early diagnosis depends upon finding rigidity in the neck and wrist, together with eye signs, and that tremor is absent in 40 per cent of victims. He also often discovers parkinsonism in patients suspected of other disorders. It is not inappropriate to mention that patients with severe parkinsonism are often alleged also to have rheumatoid arthritis, but the deformity of the hands is due to the stiffness and rigidity of parkinsonism, not to arthritis.

3. Weakness of the legs is often attributed to arthritis. One accepts disuse weakness, which will be associated with muscle wasting, but beware of the weak legs with good muscle tone and absence of wasting. Look for the upper motor neurone lesion. The knees may be arthritic, but of more serious import is the finding of an early spastic paraplegia. Since the commonest single cause is

cervical spondylosis which very frequently improves with early treatment, and since posterolateral sclerosis of the cord with addisonian megaloblastic dyshaemopoiesis may be arrested at this stage with B_{12}, it is vital to the patient that neither he nor his doctor allows arthritis to disguise a more serious condition.

STROKES

Over the age of 70, cerebral thrombosis is accepted as the commonest cause of a stroke, cerebral haemorrhage and embolism comprising most of the other causes. A severe haemorrhage is clinically obvious and carries a very high mortality with conservative treatment. This has prompted the attention of neurosurgeons, who in selected centres are now carrying out immediate cerebral angiography followed by immediate craniotomy to remove the clot and secure the bleeding point; but this is for the future. There are particular difficulties with the diagnosis of thrombosis and embolism which can only be resolved by answering the question "why did this stroke occur"?

1. Examine the cardiovascular system. Suppose you find auricular fibrillation. It is tempting to assume that here is an origin of an embolus. If the patient has rheumatic heart disease this assumption will probably be correct, but at this age the commonest cause of auricular fibrillation is hypertensive heart disease. At the onset of auricular fibrillation there may or may not be subjective disturbances to indicate the new rhythm, but the blood pressure will drop—possibly low enough to precipitate a thrombosis in sufficiently arteriosclerotic cerebral vessels.

2. Suppose you strongly suspect cerebral thrombosis but the patient is making a rapid recovery, so that you want to get her up and active, starting from the moment of full return to consciousness. If you do, a small number will react by either dropping dead, or relapsing into coma. The explanation that after one cerebral thrombosis another is likely, is not sufficient. Could sudden hypotension have been a contributory factor to the first thrombosis? If so, was a coronary thrombosis the cause? If this be missed, the patient has the triple chance of dying from either another cororany thrombosis, from cerebral embolism, or from pulonary embolism by detachment of endocardial thrombi. The moral is to study the electrocardiogram before embarking on vigorous reablement.

Two further aspects of stroke deserve mention:

3. The basis of an urgent summons is often, "Had a stroke, recovered consciousness, but cannot swallow or speak properly." Such a patient requires admission in order to ensure adequate nutrition, but before one can leave the house the anxious relatives demand a prognosis. Of two common conditions causing the foregoing symptoms, thrombosis of the posterior inferior cerebellar artery seems to me to have a far better outcome than a pseudobulbar palsy. Patients with the latter condition, having a double pyramidal lesion, seldom require less than four to six months in a hospital, and in most of my patients a parkinsonism state seems to develop which is peculiarly resistant to drug treatment.

4. The fat elderly subject with a ten-year history of diabetes mellitus, but otherwise seemingly healthy, is found one morning deeply unconscious. It is strange how often the coma is alleged to be due to diabetic ketosis, and the

unfortunate patient has 50 to 100 units of insulin pumped into him before transfer to a hospital. Apart from the fact that ketosis is rare in diabetes of late onset, it is almost impossible for ketosis to develop as rapidly as thrombosis or haemorrhage—the usual cause of the coma. Again, if the patient is not seen until more than twenty-four hours have elapsed, the smell of acetone on the breath is more likely to indicate starvation ketosis than diabetic ketosis. Such patients are emergency admissions, and it is safest to withhold insulin until the patient is hospitalized and the blood chemical picture is known.

HEART FAILURE

It is amazing how seldom a diagnosis of heart failure is supported by evidence of the cause, yet surely we have passed beyond simple empiricism and require knowledge of the basic cause of the disorders we treat? Any heart which carries a person through life to the age of 70 or over is an organ of fine quality and it does not fail without good reason. If one attributes all failure to atherosclerosis, then other causes with an infinitely better prognosis will be overlooked, and the condition will lack the appropriate treatment.

(a) *Anaemia.* Tachycardia, dyspnoea, raised venous pressure, and oedema will clear more certainly by stopping chronic haemorrhage and giving the necessary haematinics than by administration of digitalis and diuretics, which may aggravate the symptoms or add to them. Although angina pectoris of effort is rare in the elderly female, in my experience anaemia is as often to blame for the symptoms as all other causes together. How gratifying to doctor and patient when correction of the blood picture relieves all the dreaded symptoms!

(b) *Infection.* When the margin between cardiac stabilization and failure is small, the retention of sodium, due to presence of infection, may be sufficient to precipitate congestive heart failure. Vigorous treatment of the infection is often the only treatment required for the heart failure. In long-standing respiratory disorders with pulmonary hypertension an added infection may prove quickly fatal if unrecognized.

(c) *Thyrotoxicosis.* In the elderly the only manifestations may be a persistent tachycardia and a failure to maintain weight despite a good appetite and an adequate diet. The slow downhill course into congestive failure will be arrested by administration of an antithyroid preparation when digitalis by itself is impotent.

A famous aphorism of William Evans states it is possible to make two mistakes in cardiology; first, failure to diagnose heart failure when it is present; second, to diagnose heart failure when it is absent. The second is the greater hazard of cardiology in the aged. If an old person has oedema of the ankles, the chances are that heart failure will be the suggested diagnosis, and this is more likely to be incorrect than be confirmed by further examination. The commonest cause of oedema in the elderly is increased capillary permeability with which may be associated anaemia, malnutrition, or hepatic fibrosis with consequent changes in the osmotic balance between blood and tissue fluids. Moreover, immobility deprives the leg veins of the important action of leg muscles in promoting venous

return. Venous obstruction from old thrombophlebitis, varicose veins, or an unsuspected abdominal tumour, should all be excluded before the oedema is held to be renal or cardiac.

Dyspnoea, indigestion, raised jugular venous pressure, enlargement of the liver, ascites, and moist sounds in the lungs are all symptoms or signs which may accompany a failing heart and collectively offer strong support for the diagnosis, but it is equally true that individually these same symptoms and signs have a host of causes unrelated to a failing heart. Seek the truth in the heart itself. Concentrate on the heart sounds and rhythm rather than on any clamorous bruits. If the third or fourth heart sound is present, there is the firmest basis for the diagnosis of heart failure in the patient over 70. Marked tachycardia makes recognition difficult by ear alone, and there are rare benign causes of a third sound even in old age. This leads to the logical conclusion that heart failure can be diagnosed at the bedside only when at least two positive signs are present in addition to a suggestive history. Since the latter is often lacking in old people who live alone, the non-committal diagnosis of "oedema of uncertain origin" is the only safe one at the bedside, and admission to a hospital is usually required. This has the double virtue of ensuring that a cause will be diligently sought and will prevent inappropriate and possibly dangerous treatment.

GOING DOWNHILL

All of us have used this expression when either we know beyond doubt that a patient has a disorder which is invariably fatal or, uneasily, when the patient simply is not progressing and we do not know why. We review all the evidence, re-examine the patient and still wonder what we have missed. No diagnosis offers itself. If the patient dies in the hospital we ask for an autopsy and try again to find the cause of going downhill. Though there are occasional surprises, *e.g.*, a quiet peritonitis, the point of great clinical importance is that the autopsy often fails to reveal any cause of death. By virtue of age there will be some myocardial degeneration, and that becomes the certified cause of death. Doctors who are primarily scientists may feel that the whole case has been most unsatisfactory, but doctors who combine philosophy with their science know that death from nonspecified disease, or natural causes, is very common. It is a physiological end-point. This imposes an important duty on every physician. He must be able to recognize when a person is actively dying, by which I mean that the dying is irreversible under any circumstances and that a prognosis in time is possible. Why is it so important? Because the majority of relatives prefer to nurse at home their dying kinsman, once assured that no benefit could come from transfer to a hospital; removal of uncertainty from their minds enables them to tackle their responsibilities with resolution when they know that time is limited. I can think of no other condition in medicine which depends so much on personal observation, intuition, and the formation of personal criteria for accurate assessment. Any enlargement upon this would be out of place; the hazard is to forget that dying is often benign. Do not disturb them, for they are at peace.

SUMMARY

There are approximately 60,000 pensioners in the Brighton & Lewes hospital area, Sussex, England. We reckon that at any one time 10 per cent require help (6,000). Half (3,000) of these require assistance to keep them healthy, and are the responsibility of the Welfare and Public Health Services. The other half (3,000), *i.e.*, 5 per cent of all pensioners, require active medical treatment. This Unit has 333 beds of all categories for both sexes. Thus a unit bed is available for approximately only 1 in 10 of the elderly sick, so we cannot afford haphazard admissions. Whenever possible, facilities for treatment are arranged in the patient's home. The first requisite is an accurate clinical assessment, for this determines home or hospital management.

This article has a fourfold purpose:

1. To condemn categorising elderly persons as "senile," "arthritic," "paralysed," "in heart failure," or "going down-hill," as valueless for management. Common diagnostic hazards within these five groups are discussed.

2. To indicate to family doctors that the elderly are as susceptible to accurate diagnosis as younger patients.

3. To stress that bedside diagnosis in the elderly is not only possible but a necessary and fascinating exercise. Submitting elderly infirm or sick to a barrage of investigations is generally unkind, often unnecessary, and can swamp the laboratory services unless a careful self-discipline is practised.

4. To suggest that dying is a physiological end-point of healthy old age.

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THE EFFECT OF TRIETHYLENE THIOPHOSPHORAMIDE (THIOTEPA) ON MALIGNANT TUMORS*

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One of the newer drugs for the treatment of malignant tumors is triethylene thiophosphoramide, commonly known as ThioTEPA. This substance is derived from nitrogen mustard and is similar to triethylene phosphoramide (TEPA), but has a sulfur atom rather than an oxygen atom attached to the phosphorus in the molecule (Fig. 1). Its effectiveness against tumors in mice has indicated that it might be effective against tumors in human beings.

Triethylene thiophosphoramide occurs as a white hygroscopic powder. It is prepared for use by solution in distilled water at a concentration of approximately 10 milligrams per cubic centimeter. The solution may be filtered and stored in a refrigerator at 4° to 6°C.

Triethylene thiophosphoramide is not irritating and may be used in any desired manner. Experience has shown that the best effect is obtained with high concentrations of the drug within the tumor. It may be used for peripheral lesions in the lung by intravenous or intra-arterial injection. It may also be injected intramuscularly, subcutaneously, or directly into a tumor mass. Malignant conditions of the pleura and peritoneum are susceptible to injection of the substance into these cavities. The drug may be administered by repeated injection through a polyethylene catheter placed in a tumor at the time of surgery. Intramediastinal tumors are particularly susceptible to this form of therapy.

ACTION

ThioTEPA has radiation-simulating and lymphocytopenic activity. Its effect does not become apparent for five to fifteen days. The maximum effect is usually noted about the twenty-first day. The dosage of the drug must of necessity be individualized. It is controlled by the total leukocyte count and especially by the lymphocyte count, as the drug can exert a pronounced depressant effect upon hematopoiesis. The dose of ThioTEPA, like that of methyl-bis-β-chloroethylamine hydrochloride, is approximately 0.1 milligram per kilogram. In our study, the drug was used initially at this dosage level, but the quantity was reduced upon subsequent injections to an average dose of 0.05 mg. per Kg. of body weight for continued administration. Some degree of tumor control was secured through the use of the drug on a week-to-week basis by injection directly into the tumor site or intravenously.

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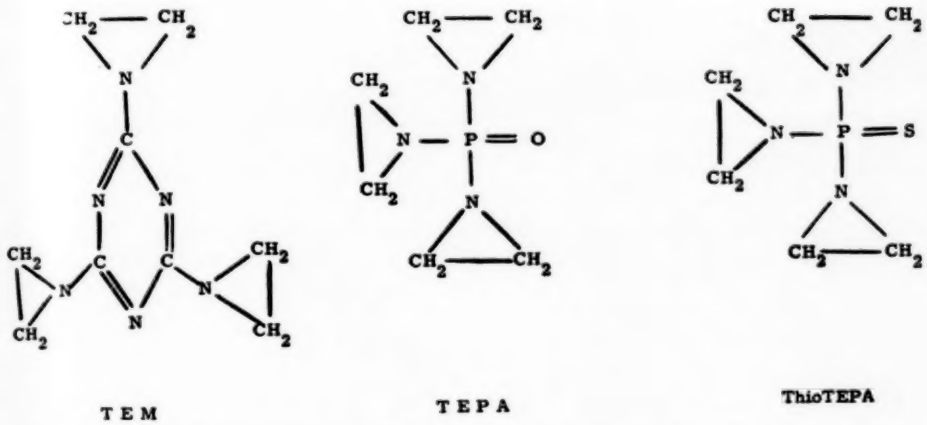

FIG. 1. Structural formulae of the mustard derivatives, triethylene melamine, triethylene phosphoramide, and triethylene thiophosphoramide.

RESULTS

The responses to ThioTEPA therapy in a variety of tumors were as follows:

Tumor	*Response*
Carcinoma of the bowel	Fair
Carcinoma of the lung	Fair
Carcinoma of the ovary	Fair
Melanoma	Fair
Carcinoma of the breast	Good
Granulocytic leukemia	Good
Hodgkin's disease	Good
Lymphosarcoma	Good
Lymphocytic leukemia	Excellent

The effects varied from fair to excellent. In general, only radiosensitive tumors were treated with this drug. The best results were noted in lymphocytic leukemias and lymphosarcomas. Good results were obtained in tumors readily accessible to local injection so that a high concentration of the drug could be obtained. Less benefit was apparent in tumors reached by the drug through intravenous injection, such as carcinomas of the lung and carcinomas of the pleura or peritoneum. Improvement in such situations was of short duration.

The drug was tried in 3 cases of melanoma. Good effects were obtained at the sites of the lesions where there was some evidence of restraint and restriction of growth. However, each patient ultimately continued his downhill course.

Figures 2 and 3 show histologic sections from a melanoma before and after the injection of ThioTEPA. As shown in Figure 2, the epithelium is a markedly hyperplastic and hyperkeratotic stratified squamous variety. In the underlying tissues, there is a diffuse solid tumor consisting of many melanophores as well as highly malignant anaplastic melanocarcinoma cells. These cells have prominent nucleoli and show little tendency to form specific structures. The vascular bed in the surrounding area was rich and the tumor was progressing rapidly.

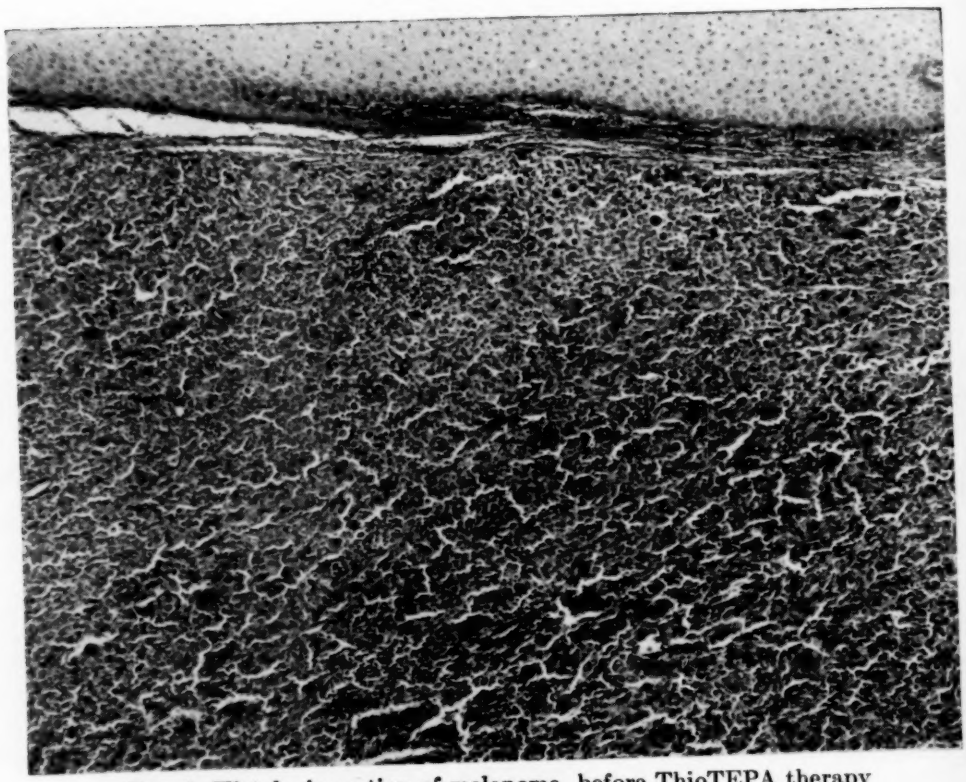

FIG. 2. Histologic section of melanoma, before ThioTEPA therapy

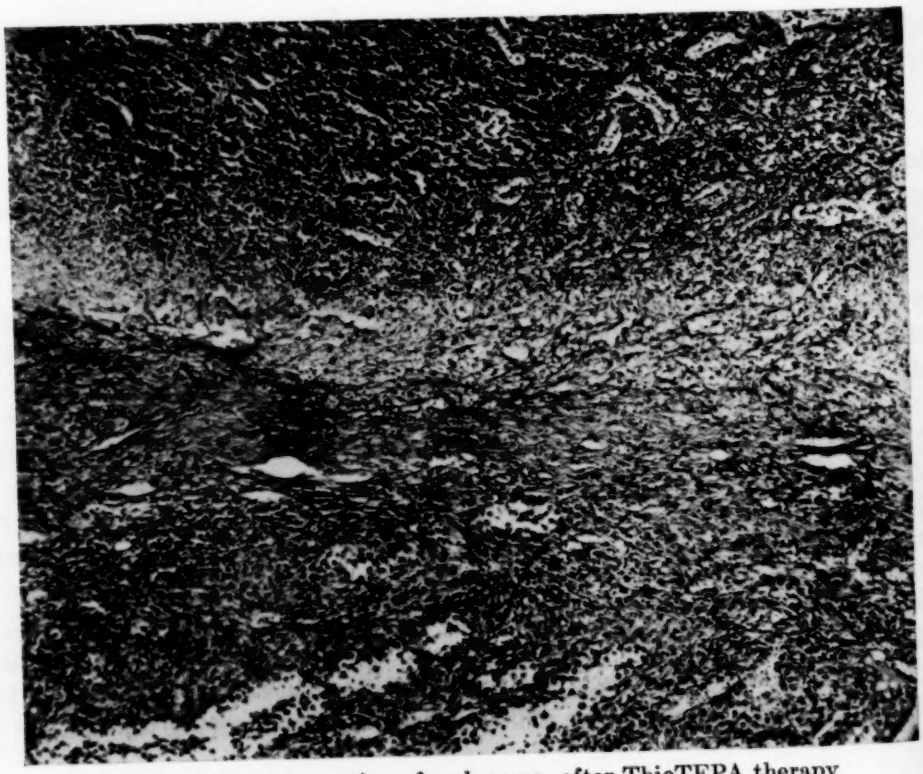

FIG. 3. Histologic section of melanoma, after ThioTEPA therapy

This particular inguinal melanoma was treated by direct injection of ThioTEPA in a dosage of 10 mg. weekly for several months. The results of this treatment can be seen in Figure 3. There is a line of demarcation between the necrotic area above and the degenerating area below. There is some production of fibroblasts between these two areas. The necrotic area is completely decimated, but tumor cells persist in the lower area. Under high power, these cells were observed to be eosinophilic, the nuclei pyknotic, and the cytoplasm swollen. There is disruption of the vascular bed because of the degenerative process and necrosis in the surrounding area.

The destructive effect of ThioTEPA in this particular tumor was readily apparent and representative of the result obtained in most of the carcinomas which were benefited. This local action of high concentrations of ThioTEPA is the most prominent and devastating effect yet seen with a carcinolytic agent of the mustard type.

Noteworthy results were obtained in carcinoma of the breast, in which direct injection of ThioTEPA into the lesion was readily accomplished. The cutaneous tumor nodules so treated could be seen grossly to regress. Some brown pigmentation of the skin appeared, but the patient had no complaints of pain or discomfort. Some tendency toward regression of the scarring process due to tumor invasion was noted in breast lesions.

The injection of ThioTEPA into the pleura and peritoneum caused some decrease in fluid production, but subsequently these lesions became unmanageable. Injection of the drug directly into mediastinal and retroperitoneal masses produced excellent results, with reduction in the size of the tumors.

One carcinoma of the bowel was treated with benefit for a limited time. Ultimately, sclerosis of the lesion and obstruction of the bowel developed.

TOXICITY

Triethylene thiophosphoramide has, in general, the same effects as methyl-bis-β-chloroethylamine hydrochloride. Initially, a fall in lymphocytes occurs after the drug is administered. This takes place within three to four days after the first injection. Subsequently, the gross white cell count falls and the lymphocyte count continues to decrease. If the drug is continued, there is a reduction in total leukocytes with further reduction in the granulocytes. If this is allowed to continue, a fall in reticulocytes and platelets is also observed. In several patients, there was severe depression of the bone marrow as well as a reduction in platelet count. Patients showing these effects should be treated with platelet transfusions; one such transfusion usually suffices to overcome the toxic effects. The patient will usually show an increase in platelets and then a gradual increase in granulocytes and lymphocytes within a week after the medication is withdrawn. After two to three weeks, no further toxic effects will be noted and spontaneous regeneration can occur.

SUMMARY

Triethylene thiophosphoramide (ThioTEPA) was used for approximately nine months with beneficial effects in carcinoma of the breast, lung and ovary,

and with some degree of improvement in melanoma. The result was excellent in lymphocytic leukemia, but less pronounced in lymphosarcoma, Hodgkin's disease, and granulocytic leukemia. Although the medication is safe in general, its use must be carefully correlated with hematologic studies, as it exerts a markedly depressant effect upon hematopoiesis. If the dosage is reduced, the drug may be continued at a lower level without ill effect. It is effective when injected directly into a tumor and the results are excellent when a high concentration can be attained.

SOCIAL AND ECONOMIC ASPECTS OF OLD AGE*

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It seems to me, as I read the literature and participate in this conference and in others here and abroad, that too many people in the medical and biologic fields view aging solely as a set of biologic processes occurring within the organism. There appears to be a lack of recognition of other changes that take place in the life of the individual with the passage of time. There is also a lack of awareness of changes that are taking place in our culture that have a bearing on the situation.

Research into the nature of the changes that occur in the structure and in the performance of the organism is essential, and should be pursued with all possible vigor. Likewise, research on disease processes and medical services is designed to promote optimum health and to control disease among older people.

What concerns me is that some who are pioneering brilliantly in these fields are willing to state that all of our effort, all of our research, should be directed towards these ends. The assumption appears to be that, if we keep the individual healthy, he will continue to function independently and there will be no other problems. Some do seem to recognize other facets of life, but appear to feel that the nonmedical problems of aging can be solved by a common sense "off the-cuff" manner, or by adherence to principles evolved in earlier cultures.

The point of view I have outlined is applicable to lower animals. Man, however, as we all know, is more than a biologic creature. He also has a psychosocial life cycle, and he is aging in a rapidly changing cultural environment.

It may appear that I have been at pains to set up a straw man in preparation for knocking him down. In part, this is true. On the other hand, I know that many people in the medical fraternity recognize aspects of aging beyond those found in the biologic organism. More important, most of you are well aware of the two-way relationship between certain physiologic and sociologic phenomena. The invitation I received to participate in this symposium is an example of this recognition.

My purpose is to demonstrate that there are aspects of aging that have to do with man as a social being, and that these phenomena can be examined scientifically; that is, they can be measured, they can be related to one another, and it is possible to predict one from another. These, I believe, are the principle criteria of the scientific method.

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There are quite clearly two phases of the social phenomenon of aging, the societal and the individual. Aging is a phenomenon of the group, or of society, and has implications for group life. There are also social changes in the life of the individual. The two phases are closely related. I shall, however, focus on the societal aspect.

I wish to discuss briefly the changing number of older people, the growing freedom from traditional adult roles, the manner of employment and occupation, family relationships, and the question of financial support.

How many older people are there, and why?

We are all familiar with the large numbers of older people in the population of the United States—nearly 40 million persons between the ages of 40 and 69 years and 9 million 70 years of age or over.

We have fallen into the habit of explaining their very rapid growth in terms of increasing life expectancy, based upon improvements in the health environment including medical care. Actually, the increase since 1900 derives mainly from the natural increase in the population, that is, from the number of births that took place between 1860 and 1890, less the number of deaths since 1860. Although the birth rate was declining during that period, the population had been growing and there was a rising number of children. These children, with death rates at the 1900 level, account for about 50 per cent of the increase in the older population during the last fifty years or so.

Immigration has also played a sizable role. Large numbers of young and middle-aged people, up to a million a year, came to the United States prior to World War I. These people, too, have aged and account for about 20 per cent of the increase since 1900.

Health improvements, sanitation, nutrition, and new medical and surgical procedures take care of the remainder of the increase—30 per cent. This factor is assuming increasing importance as time goes on.

The Bureau of the Census has calculated the influence of these several factors quite exactly. Moreover, the Census has made some rather secure predictions covering the remainder of the century. Thus, by 1975 there will be at least 50 million middle-aged persons—45 to 69 years of age—and 13 million aged 70 years or older. Today's 14 million aged 65 years and over, will increase to about 27 million by the year 2000.

These estimates are obtained by the simple procedure of applying current death rates to the population now alive. Those who will be age 65 in the year 2000 are 20 years old today. These estimates are, however, subject to some uncertainty. There is no way to predict just how much farther increase in life expectancy may result from the research and new technics now being developed and applied.

Changes in the way of life

There is another factor in aging, as yet little recognized but just as real in creating the present situation. Not only are there more older people but also,

perhaps even more important, older people are living in an entirely different society from that in which they were born. The changes that have taken place have profound implications for our approaches to aging.

Traditionally, man's life has been devoted to making a living, reproducing himself, and preparing his children for their adult roles. Most human activity has focused on these occupations. Men, and women too, have worked many hours a day over their entire lifetimes. Retirement has been virtually unknown, except for the aged and sick. These things are not true of modern society. Machines have largely taken the place of the hand tools of our forefathers. New forms of energy have almost replaced the human and animal energy that supplied the power in colonial days.

The shift to mechanization has been dramatic. In 1850, 10 billion horsepower-hours of energy, or 440 hours per capita, were used in supplying the needs of the population of that year. This year—1955—nearly 700 billion horsepower-hours, or 4,500 hours per capita, will be utilized in fulfilling our wants for goods and services of all kinds. Another contrast is that, in 1850 some 65 per cent of the energy was supplied by human muscles and by animals. Today only 2 per cent comes from these sources, and 98 per cent from fuels and water power.

The consequences of these shifts have revolutionized our way of life. In primitive and colonial days, the household was the center of work and family activity. The living was made in the household. Food was grown and prepared. Clothing was made at home. Children were educated there and cared for when sick.

This way of life has changed markedly as a result of industrialization. The three-generation household has all but disappeared. Most of us earn our living away from home. Food, almost ready for use, is assembled from stores. Clothing is purchased ready-made. Education, recreation, and religious instruction are provided in community institutions. Sickness among children has all but disappeared and most serious illness is treated in hospitals. As a result, the three-generation household is no longer needed.

When children set up their own families, they are largely self-sufficient. Parents at age 45 to 55 years have discharged their parental responsibilities and are free to focus on new interests. Thus, one of the traditional, lifelong roles of adulthood is completed in middle age, while a quarter of a century of life remains.

There are other changes. Work for most people is much easier and occupies less of their time. The forty-hour week is only a little more than half the length of the work week three or four generations ago. We are now able to look forward to a period of complete retirement from work. At the turn of the century, 30 per cent of the men 65 years and over had retired from the work force. Today, the proportion is 60 per cent. Thus, we are also tapering off or completing our work roles, well in advance of the end of life.

The changes that I have described in our ways of life are profound. Although they affect all aspects of our lives, I believe they have special significance for middle age and later adulthood.

I think they permit us to write a sociologic definition of aging—"more people living longer, coupled with the completion of adult roles at relatively earlier ages."

So complete has been the shift from the pattern of pre-industrial society that we may say we have, in truth, created a new period of life, a period marked by increasing freedom from traditional responsibilities, with opportunity for the development of new interests and activities.

Moreover, we can predict that the process will continue; we are seeing only the beginning. New machines and new sources of power are moving our productivity to new, higher levels, day by day. It has been estimated that if the rate of increase of the past fifty years continues to the year 2050, the length of the working week will be seven hours. Although no one is actually making such a prediction, there is every reason to believe that we shall be working thirty-five hours per week or less within the next decade or so. Likewise, some economists feel confident that the proportion of men over 65 years of age who are retired from the work force will rise still further, particularly after the children of the 1940's reach their productive years and move into the work force.

These new developments raise a number of important questions. The key question, perhaps, is what to do with the time freed by our technological culture. Vigorous efforts are being made to break down barriers to the employment of middle-aged workers and to do away with the archaic practice of retirement at a fixed chronologic age. Even though these efforts should succeed, there will be millions of older citizens not devoting the major part of their time to paid employment.

New roles

The great challenge, it seems to me, is to find new roles and occupations to replace those that are being completed. We have created leisure because we have wanted it. What shall we do with it? Some people are finding new and exciting experiences in education, in creative activities, in new kinds of services to people. Others who have not made the adjustment are withdrawing from community life and are cluttering up physicians' waiting rooms.

Family relationships

The relationships and responsibilities of the younger and older adult generations toward each other have become another area of concern. It was noted earlier that the multi-generation household, necessary in pre-industrial society, has broken down into its components of small family units as a process of adaptation to our mechanized urban economy. One measure of this change is found in the fact that, during the last twenty-five years, the number of family units has increased twice as rapidly as the population.

Recent research has shown that there is mutual agreement to the separation of the generations. Young adults, occupied with their own children and relationships, living in small dwellings, and highly mobile, have little need or desire for the older generation within the immediate family unit. Those of the older generation appear to want the freedom, self-sufficiency, and security of their own homes.

Because most people remain gainfully employed until 60 or 70 years of age, and

because retirement pensions are becoming increasingly common, the majority of older persons are able to maintain separate living establishments. Eventually, however, many encounter problems. When widowhood or retirement from work overtakes them, they are likely to experience a good deal of loneliness and even social isolation. When they become frail or severely disabled by long-term illness they may no longer be able to maintain a separate existence.

We are now beginning to see the implications of these family changes. We recognize that the fairly common practice of urging children to provide accommodation for aged parents is leading to a good deal of unhappiness and even family discord. It is becoming obvious that new kinds of living arrangements are necessary—small dwelling units, residence clubs, boarding homes, group dwelling units, and perhaps retirement villages, supplemented with home services and community facilities for maintaining active lives and human contacts.

Can the economy support the new generation?

Another question causing all of us a good deal of concern is whether or not the economy can afford a constantly-growing retired population. This may appear to be a fairly simple question. Yet, it is a particularly involved one. Nevertheless, social science has some data to offer.

The readiest answer is that for fifty years we have been affording more older people and deriving other benefits as well. The older population has quadrupled since 1900, and the proportion of these larger numbers who are retired has doubled. We have already seen that we have greatly reduced the hours of work over the same period. Yet, strange as it may seem, we have also doubled our level of living.

The income available to each of us (per capita income) in dollars of constant value is almost twice what it was in 1900. This is another consequence, largely of our scientific and technological civilization.

There has been one more factor. Until recently, the declining birth rate more than offset the rising number of older people. Hence, for more than fifty years we had a declining ratio of dependents to persons in the productive age period. This trend has been reversed, however, since our young people have recently decided to have more children. Yet, it seems likely that the ratio of dependents to persons in the productive years of life will not increase markedly during the remainder of the century.

It has already been stated that new processes and new forms of mechanical power will bring a continuing increase in worker productivity, even though the hours of work are shortened still further.

On the basis of available data, economists have estimated that per capita income will rise by 20 per cent during the next decade, and that it will double again over the second half of the century.

Thus, on the assumption that we shall be able to keep the economy at a high level of operation, the same forces that are giving us longer life and more time for ourselves will also give us a continuously rising level of living. Hence, the retired population, so far as we are able to foresee, should not prove to be an insur-

mountable burden. However, any marked rise in services to the aged might alter such a conclusion.

Finally, it should be observed that modern methods of saving, and the growth of various types of insurance, mean that increasingly the retired will be living on their own deferred earnings and not on contributions of the younger generation. This, in fact, is true of 60 per cent of the older population today.

In conclusion, I have tried to show that there is a socio-economic phenomenon of aging as well as a biologic process. Furthermore, this new development in our culture is measurable and predictable from underlying factors. We have, in fact created a new period of life which in turn creates problems in occupation, family relationships, living arrangements, and financial support. Extended research in these areas is needed fully as much as in the biologic and health sciences.

DRUG THERAPY IN ANGINA PECTORIS

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Since the classic description of angina pectoris by William Heberden (1) in 1772, great effort has been expended in the search for drugs which may exert benefit in the management of this syndrome. Although some early investigators expressed little faith in treatment, others prescribed a variety of agents in either the belief or ambitious hope that significant relief could be achieved. Heberden himself exhibited conservatism in advocating only quiet, warmth, "spiritous liquors" and opium. Similar restraint was not practiced by others, who frequently prescribed "issues," "blisters," antimonial and mercurial alteratives, the volatile tincture of guaiac with antimonial wine, laxatives, tar water, Peruvian bark, the fetid gums, camphor, extract of hemlock, spirits of nitrous ether, chloroform inhalations, Hoffman's anodyne, strychnine, bromides, quinine, digitalis, carminatives, colchicum, iron, arsenic and belladonna (2). In 1867 Brunton (3) reported on the use of amyl nitrite and in 1879 Murrell (4) indicated that equally successful results could be obtained with nitroglycerine.

A casual glance over the past several decades also brings to mind one drug after another which has had its little day of popularity only to sink into mute oblivion. The failure to recognize fully the high effectiveness of placebos in treating subjective ailments has brought into prominence numerous medicaments for the treatment of angina pectoris which in themselves are totally lacking in specific effects. It is now widely recognized that relief of pain in angina pectoris may be achieved not only through the influence of vasodilator drugs and agents which favorably affect myocardial efficiency but also in response to medicaments such as placebos or analgesics which act solely on the psychic reaction to pain perception (5). Awareness also exists that many patients respond to the "ceremony of therapy" and that results are often proportional to the enthusiasm with which medication is prescribed. In an effort to control such possible sources of error, the "double blind" technic in which the identities of a test drug and placebo remain unknown to the patient and physician until the analysis of the data is completed, is now widely utilized and regarded as indispensable (6). Some, however, maintain that the method is of no value in distinguishing known potent agents from inert substances (7). Without undeniable proof, such failure must be regarded as an indictment not of the technic but of the design of the clinical experiment to which it is applied. Indeed, the vagaries influencing the anginal state require that observations of the effect of drugs should be made for a minimum of one year in large groups of patients (8). Moreover, in evaluating the action of a drug, placebo-reactive patients must be separated from placebo-nonreactive patients in order to insure a high level of accuracy. Since such conditions are rarely if ever satisfied in drug evaluations, the validity of the findings

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reported are open to question. When all requirements are met, "double blind" studies may successfully identify potent analgesic drugs or effective coronary vasodilator agents, but remain valueless in the differentiation of one group from the other.

One may ask whether the patient with angina of effort who responds to a placebo or analgesic is given the same measure of protection by these agents as by nitroglycerine. Relief of pain by any effective means is no longer permissible in the treatment of this disease. The thoughtful physician seeks to control this symptom by prescribing a drug which eliminates the pain-producing myocardial hypoxia. He regards any other method of pain control as secondary to this main therapeutic objective. Consequently, drugs which relieve angina by affecting the anatomic apparatus of pain or the psychic reaction to its perception must be clearly differentiated from those acting specifically on its initiating stimulus.

Since the criterion of pain, at best, is notoriously deceptive, some have utilized methods based upon the ability of specific agents to modify the electrocardiographic response to standard exercise in carefully selected patients (9–15). The validity of such evaluations is supported by various findings. Electrocardiographic configurations evoked by an exercise test are similar to those commonly recorded during spontaneous attacks of angina pectoris in the same patients. Moreover, it has been clearly established that glyceryl trinitrate can prevent or abolish these electrocardiographic patterns, whether occurring spontaneously or artificially induced in the laboratory. The method, therefore, permits the identification and assay of drugs which mimic the action of glyceryl trinitrate in its influence on electrocardiographic patterns. It affords a means of determining whether or not relief of angina detected in "double blind" clinical studies is mediated through analgesic action or through a specific influence on coronary-myocardial relationship. The technic eliminates the problem of the placebo reactor and the distorting influence of psychic factors involved in all evaluations based upon the index of pain. By such objective studies, it has been shown that alcohol fails to reduce the disparity between coronary flow and myocardial requirements (10). Consequently, like morphine, alcohol relieves pain solely as a result of a sedative action. Evaluations of over 20 of the commonly used "vasodilators" showed that only glyceryl trinitrate, papaverine (in massive dosage, 3 to 8 grains) and pentaerythritol (Peritrate) tetranitrate elicited an impressive response when studied in this manner. The results obtained with triethanolamine (Metamine) trinitrate biphosphate, dioxyline (Paveril) phosphate and Nitroglyn (glyceryl trinitrate in specially coated granules), respectively, were in sharp contrast with these findings (15). Similarly, administration of aminophylline, Roniacol (beta-pyridyl-carbinol tartrate), tolazoline (Priscoline) hydrochloride tetraethylammonium chloride, octyl nitrite, visammin (khellin), heparin, bishydroxycoumarin (Dicumarol) and choline (Choledyl) theophyllinate did not induce a significant response when evaluated by objective criteria based on exercise-electrocardiograhpic tests (14).

In the absence of drugs which infallibly prevent the initiating stimulus for angina, the value of analgesic and tranquillizing agents should be clearly recognized

in the management of this disease. Although drugs given for pain, like placebos or analgesics, are stated to affect the reaction and not the stimulus, in angina pectoris this is not entirely true. It is perhaps unique that in this disorder, the reaction tends to perpetuate or augment the original stimulus by increasing metabolism, blood pressure and heart rate and by decreasing cardiac efficiency. Since these effects are mediated through the sympathetic nervous system and catechol amines, the greater the psychic reaction to pain the greater must be the "rebound" tending to augment the imbalance between coronary flow and myocardial requirements. Consequently, in patients in whom pain cannot be controlled by currently available "vasodilators" there would appear to be a real place for analgesic and tranquillizing agents.

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GERIATRIC ASPECTS OF FRACTURES IN THE INSANE

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This report is based on observations in 267 fractures of the humerus and hip which were treated during the period of 1950–1955 at the Milledgeville State Hospital. It has a twofold aim: 1) to discuss fractures in the aged, especially those of the hip, with their geriatric complications, and 2) to outline the management of these problems in the insane.

At no time in the past has the medical profession been called upon to treat so great a number of aged patients. People are living longer than ever before and we are being forced to recognize that geriatrics is rapidly becoming a separate department in medicine. In the United States there are now 6,000,000 more persons who are 65 years of age or older, than there were in 1900 and it is estimated that by 1980 the total number of those in this age group will be 22,000,000.

In this group of persons we expect to encounter the naturally occurring infirmities of old age and the increased incidence of accident. Of these accidents we shall discuss only fractures of the surgical neck and shaft of the humerus and fractures of the hip.

In the management of these fractures our selection of the type of treatment is guided largely by both the general physical condition and the mental status of the patient. In some cases the fracture has had to be ignored because of the predominance of some other accompanying condition.

FRACTURES OF THE HUMERUS

In fractures of the surgical neck and shaft of the humerus in geriatric insane patients, we frequently have to abandon the idea of any type of cast because of such factors as debilitation, cardiac decompensation and the ever-present susceptibility toward pneumonia. In this age group, the shoulder spica with the arm in abduction in the so-called "airplane" splint is practically prohibited by the inability of the patient to manage himself so encumbered. Traction is often impractical, due either to the violent nature of the patient, his inability to cooperate, or his poor physical condition; however, a few patients permit the use of skeletal traction followed by the application of a light cast in the Velpeau fashion. In the more uncooperative patients who may be ambulatory, we also apply this type of cast after all possible reduction has been attained. Another group of our humeral cases have done well after an open reduction and fixation by metal plate and screw, or internal fixation with a medullary pin. Still another group has done well with no treatment.

FRACTURES OF THE HIP

Fracture of the hip is an injury very frequently met with in the old age group. It is my opinion that nowhere in practice are the problems and complications

due to age so acutely manifested as in fractures of the hip; and furthermore, nowhere is the incidence of this injury so great as in senile, psychotic subjects. Many hip fractures are the results of the patient's own violence. Others are the result of falls caused by senile weakness and lack of coordination and equilibrium, which may in turn be due to arterial changes characteristic of senility. Another group of hip fractures is the pathologic type which may result from bone disease such as osteoporosis or osteomalacia, senile bone atrophy, or secondary metastatic tumors.

There are often pre-existing conditions to which the patient may have become adjusted for some time; these conditions may become increasingly severe following the added burden placed upon the body by the fracture. Often we see a rapid progression of myocardial failure, peripheral circulatory collapse, or diabetic coma. We have also seen deaths due to pulmonary infarction following the fracture, even when there had been no surgical intervention. Many of these patients are arteriosclerotic. Cerebrovascular accidents have occurred with resulting hemiplegia. In hip fracture cases, when the cerebrovascular accident has been thought to be due to cerebral thrombosis, we have performed a stellate-ganglion block. Twelve such patients had return of function but were unsuitable for active treatment of the hip. Malnutrition is an outstanding condition in this age group. Decubitus ulcers often present a serious handicap in treatment of the fracture. Following the fracture the bedsores usually increase in size, number and severity. Renal failure ensues in a moderate number of cases and such patients may pass into coma and die before any treatment of the hip is feasible. The conditions attending senility are considered in the recent concepts as not being diseases per se, but natural degenerative processes which are physiologic and consistent with old age; however, they render the recuperative powers of the entire body less flexible, and minimize the scope of repair and regeneration.

TREATMENT

In recognition of these problems of senility and insanity, for treatment we divide fractures into five groups.

1. Operative cases, involving open reduction and fixation with a Smith-Peterson nail, with or without an intertrochanteric plate.

2. Traction cases, comminuted to an extent in which the nail is not feasible, and the patient is unable to withstand surgery. Skeletal traction is usually applied by inserting a Kirschner wire through the tibia near the tubercle. We seldom have had to employ this method.

3. Cast cases. Bilateral hip spica is used in extremely psychotic patients, in the absence of bed sores, and when physical condition permits. Fortunately, this is rarely indicated.

4. Cases in which no definite treatment is used, due to severe complications.

5. Cases treated with a prosthetic femoral head. We have used the Austin Moore prosthesis in 6 cases which showed complete absorption of the femoral neck. This restored length and adequate function. Each of these patients was walking unassisted within one month after operation.

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4. Cases in which no definite treatment is used, due to severe complications.

5. Cases treated with a prosthetic femoral head. We have used the Austin Moore prosthesis in 6 cases which showed complete absorption of the femoral neck. This restored length and adequate function. Each of these patients was walking unassisted within one month after operation.

In fractures of the femoral neck which have not been nailed, non-union with absorption is far more common than in the other types of hip fracture. The intertrochanteric and subtrochanteric fractures usually heal. However, we have found during the past year that if femoral-neck fractures are nailed, there are few cases of non-union. This may be attributed to the fact that the patients who are operated upon are usually less debilitated; moreover, the nailing process affords fixation and may serve as a stimulation toward healing. We have attempted to insert the nail in a position not lower than the center of the head of femur in order to avoid injury to the ligamentum teres and its accompanying artery at its attachment at the fovea capitis femoris situated in the lower half of the femoral head.

Detection and treatment of complications, maintenance of adequate nutrition, and rehabilitation are of prime importance in the treatment of these fractures in the aged. Whether or not there has been an operation, we make periodic determinations of the levels of serum protein, and nonprotein nitrogen and of fasting blood sugar. We give blood transfusions freely. Multivitamins, thiamine, vitamin B_{12} and liver extract are administered routinely with a high protein diet. Poor appetite is a fairly constant finding, and the diet is often supplemented by an egg milk-shake, three times daily, to which has been added some form of protein hydrolysate. Poor appetite in some patients is due to the advent of a psychotic episode. Electric shock treatments have been of benefit in the restoration of appetite in selected cases.

Early ambulation is encouraged in all whose condition permits. Even in patients with non-union and absorption of the femoral neck, we attempt to get them out of bed, give them crutches and encourage them to take full steps with the affected leg and simulate walking. We have been considerably impressed by the ability of patients to bear weight on their ligaments, joint capsule, and muscle in the presence of non-union. I am reminded of the case of a 70-year-old woman who had been totally bed ridden for one year due to absorption and non-union of the femoral neck. After three months of gradually increased activity, she was able to get out of bed and walk with crutches unassisted. Rehabilitation in certain cases can become a tedious process. The patient must be able to cooperate to at least a moderate degree. We have made considerable use of the Balkan frame over the bed, to which may be fastened one or more trapezes, for pulling up with the arms. Pulleys are attached through which a rope can be run to the foot or to a Thomas splint, with or without a Pearson attachment. Thus the patient may pull up his own foot with the other end of the rope and accomplish considerable joint motion and general exercise.

One striking feature found frequently in fractures in the insane is the total absence of the perception of pain. I have reduced compound fractures with debridement, without any anesthesia. I was much impressed the first time I treated such a case. The patient was an old lady with a fracture of the surgical neck of the humerus, which was threatening to become compounded because of her activity. I manipulated the shoulder, exerted considerable manual traction and placed the shoulder and arm in a cast without anesthesia. All the while she

continued to sing and laugh in unbroken merriment. The amount of morphine required for the senile psychotic patients is a remarkably small quantity, even after there has been an operation on the hip. Also they are not as prone as sane people to shock and fainting reactions following injury. I have seen 3 patients who insisted on continuous walking shortly after their hips were fractured, when shortening of the leg was apparent. They continued in their usual manner with their usual delusions and their behavior reflected no pain.

CONCLUSIONS

It is the opinion of the writer that the foregoing principles may find practical application in *sane* patients also. With the increasing number in the old age group, we can expect an accompanying increase in the disabilities brought about by time and can expect to have more geriatric problems than ever before. The problems are many, and it is more socially and economically important to observe these principles in the *sane* group than in the *insane*. We have to concentrate more on the sane group in order to maintain them as useful citizens. Their care requires more than a stereotyped routine. Each patient is a separate entity. His personality has become fixed by the years, and this must be understood in order to gain his cooperation for treatment. We must be ever mindful that senility is attended by many natural degenerative changes, if trauma is added, there can be an upset of the delicate balances within the body. It is, therefore, of great importance that the orthopedist treating fractures in the aged have a working knowledge of "normal" senile physiology.

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THE TREATMENT OF PULMONARY EMPHYSEMA IN THE ELDERLY

The Hazard of "Conserving the Energies of Older People," With Special Refrence to Pathogenic and Allied Factors in Pulmonary Emphysema

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The concept of conserving the energies of older people has almost become a slogan, but the hazard of following this concept has become apparent in recent years, since lack of use leads to atrophy, not only of the muscular system but probably also of more complex glandular and psychologic functions. Necropsies performed by Monroe at the Peter Bent Brigham Hospital on patients with diagnoses of pulmonary emphysema or heart disease at times revealed no trace of these clinical entities, but simply a wasting process caused by atrophy—an inevitable end-result of excessive devotion to the thesis of conservation of energy. Cardiologists are indeed now proclaiming that people are being killed by rest in bed. That the pulmonary reserve of men in middle age may be markedly diminished by a lack of exercise is often revealed by the conspicuous restoration of function after the use of a new program of exercise.

Among the factors discussed in the pathogenesis of pulmonary emphysema, constitutional or inherited weakness of pulmonary parenchyma and infection of the bronchi and lungs have been prominently listed. The military posture has been indicted by Heckscher as an actual cause of pulmonary emphysema. The erect position with the shoulders drawn back and the "guts" sucked in unmistakably is a handicap to physical exertion and in itself produces increasing shortness of breath in chronic pulmonary illness. Disuse of the lungs has also been proposed by Rappaport and Mayer as a cause of pulmonary emphysema. Although their broad assumption cannot be admitted into the group of factors concerned in the actual pathogenesis of the disease, it is clear that a lack of exercise is followed by a fall in pulmonary and cardiac reserve in pulmonary emphysema.

For men to experience alarm is said by Selye to be of advantage in the maintenance of function of the adrenal glands, a point of view consistent with our clinical findings that the prescription of a life too pastoral leads to increasing tension, anxiety, hyperventilation, and consequently to the evolution of a bored, unhappy, tense state. The Chinese proverb, "Boredom tires a woman but ruins a man," should be kept in mind when physicians advocate the wholesale prohibition of alcohol and tobacco as well as the suppression of the natural craving for excitement. The adrenal glands of the rat show a conspicuous atrophy after six

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months of living under the best possible environmental conditions provided for a caged animal.

No organized psychoanalytic investigation has been made of patients with pulmonary emphysema. However, emotional factors may play a role in the etiology of asthmatic dyspnea and it would also appear that a specific emotional situation may be found in patients with bronchial asthma.

Bronchospasm of allergic origin is at times found in emphysema, so that it is of interest to review briefly the investigations of the Chicago School for Pshcyoanalysis. Federn and Weiss suggested that the asthmatic attack is a reaction to the danger of separation from the mother or loss of the mother's love. French summarized his conclusions as follows: "Asthmatic attacks tend to be precipitated by situations that threaten to separate the patient from some mother figure. The separation fear may be of actual physical separation; more frequently it is the danger of estrangement from the parental figure due to some temptation to which the patient is exposed. In such a situation the asthma attack seems to have the significance of a suppressed cry. . . . The infant's cry is at first a physiological response whose function is the establishment of breathing at birth. Very soon it acquires also a psychological meaning as a reaction of helplessness in the face of needs which the infant is unable to satisfy. After a time the infant learns that crying brings the mother and the cry becomes then a secondary means to bring the comforting mother to his side. Thus, the primary psychological meaning of crying is a reaction to helplessness in the face of an overwhelming mass of excitation which the ego is powerless to master. . . . Fear of losing the mother, however, is a motive that is by no means specific for asthma, and is in fact one of the most potent motives leading to the repression of the oedipus complex, especially in girls and in the sons of sexually repressed mothers. . . . It is of course highly probable that the answer to these questions will be found in part in the hereditary emotional patterns of these patients which we might expect to be intimately associated with their hereditary predisposition to allergic hypersensitivity."

Franz Alexander who participated in this series of investigations has expressed a similar attitude: "The question arises whether or not individuals, who later are likely to develop asthma, may have a constitutional peculiarity manifesting itself in the difficulty of separation from the mother organism first biologically and later in an emotional sense." The asthma attack is therefore an expression of a protest against separation, that is to say against securing the needed oxygen independently by breathing, and corresponds to a regressive attachment to the mother.

In some asthma patients, the childish habit of holding the breath is also found. I have described in a psychoanalytic novel the case history of a man who stammered and whose regressive attachment to the mother was the basis for a special kind of breath-holding during stammering[1]. Alexander is fully aware of the speculative nature of these considerations but produces evidence to suggest that the threshold for allergic sensitiveness is dependent upon the emotional state of the patient.

[1] Coignard, J.: The Spectacle of a Man, ed. 3. New York, Duell, Sloane and Pearce, 1941.

In a review by George Wilson of therapeutic results in 19 psychoanalytically treated patients, 9 were found to have become symptom-free, 8 were much improved, and 2 were unchanged at the time of the report. These results were not considered final proof of their hypothesis, as insufficient time had elapsed following the completion of treatment.

I have observed 1 patient with pulmonary emphysema in whom psychoanalytic therapy apparently resulted in a surprising degree of clinical benefit; an outstanding effect was a decreasing need for bronchodilator aerosols, as if the bronchiolar tonus of the hypertrophied bronchial muscles were lessened. In addition, the patient rarely allowed herself hyperventilation as a manifestation of tension. The volume of breathing when walking seemed to be less than that formerly provoked by anxiety.

Although the results of psychotherapy in pulmonary emphysema are difficult to appraise and appear less significant than symptomatic relief, one should keep an open mind concerning its use in interested patients to whom this approach appears feasible.

TREATMENT

The following recommendations for the treatment of pulmonary emphysema are based upon pathogenic and allied factors:

The patient with pulmonary emphysema should undertake exercise and build up his pulmonary reserve by employing a walking program while breathing 10 liters of oxygen per minute through a plastic cannula. This method of walking combined with oxygen inhalation has proved to be a procedure by which, in many instances, bodily fitness may be improved and cardiopulmonary function benefited so that the patient may subsequently exercise with less shortness of breath during the inhalation of air. Continuous oxygen treatment itself is one of the most valuable remedies for the patient with pulmonary emphysema. High concentrations of oxygen are not administered except when indicated physiologically, but moderate concentrations in a graduated program have been employed with evidence of value to the patient during more than two decades of experience. A relatively new advance is the program of exercising with oxygen.

The use of prednisone, a new corticosteroid, in pulmonary emphysema makes possible an increased amount of exertion and has proved of value in the treatment of more than 100 patients with the disease. It should be borne in mind that an increased amount of activity may require the use of other measures which reduce overdistention of the lungs. Diaphragmatic breathing and allied breathing exercises, and the use of the physiologically designed Gordon-Barach emphysema belt aid the program of restoration of physical fitness.

The ideal that should be sought is, therefore, the reverse of a program based on "conservation of energies" which allows these patients who are often crippled by inertia due to the hypoxic nature of the disease, to waste away, going from chair to bed and back again.

The problem of chronic pulmonary disease is frequently so complicated that a detailed regimen of treatment is highly desirable. This entails outlining the

activities during the day which are apt to be of aid to the patient in the relief of bronchospasm, the elimination of secretions, the reduction of an overdistended lung, the meticulous dedication to an oxygen exercise program, the avoidance of infection, the administration of indicated hormonal therapy, and cultivation of the proper attitude of the mind with which to meet his illness and his restricted mode of life.

There is no prescription for an attitude of mind. That is a matter of the soul of the patient as well as of the physician. The soul requires no knowledge, but simply wisdom—the wisdom of learning how to live a warm human life. Among the things that stimulate the human soul is the observation of individual progress, the inevitable result of well directed effort. Long ago it was realized that the patient with diabetes mellitus should understand the disease almost as well as the physician, as Joslin pointed out. It is now becoming evident that the patient with pulmonary emphysema should be informed as to the mechanics of breathing and ways in which he may aid the restoration of this function. The physician is better equipped to aid in this progress if he is willing to abandon the notion of conservation of the energies of older people as an untrustworthy slogan conducive to atrophy and invalidism, and to teach instead the gospel of increasing physical and mental fitness to the limit of capability. It should be recognized that fatigue is the natural result of the expenditure of energy and not productive of "toxins" but ultimately of the capacity for renewed energy.

The importance of keeping the older patient active and giving him hope deserves special emphasis. Apropos of this proposal is a quotation from Tennyson's "Ulysses":

> Old age hath yet his honor and
> his toil;
> Death closes all: but something
> ere the end,
> Some work of noble note, may yet
> be done,
> Not unbecoming men that strove
> with Gods.

MULTIPLE SERUM PROTEIDOGRAMS, LIPIDOGRAMS AND GLUCIDOGRAMS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION*

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Many efforts have been made to diagnose atherosclerosis or, more specifically, to detect signs of pending myocardial infarction. A host of chemical, physicochemical, physical and clinical tests have been claimed to yield results indicative of threatened infarction. Recurrent infarction can be anticipated on the basis of statistics. A method of predicting the first attack of myocardial infarction has yet to be found.

It has been postulated that alterations observed during an episode of acute myocardial infarction might furnish a clue to prodromal signs. Our study was designed to find such a base line for surveillance of patients in the latent period between acute attacks.

MATERIALS AND METHODS

Thirty patients hospitalized for acute myocardial infarction were studied. Diagnosis was established by all available clinical, physical, and laboratory methods. Patients were re-examined regularly during hospitalization. All patients were given oxygen, and all received commonly applied medication. Half of them were treated with digitalis, and half with dicoumarol. In 8 patients, digitalis and dicoumarol medication overlapped. (Patients treated with heparin were not included in this series.)

Blood was withdrawn promptly upon hospitalization. In 1 patient the first blood sample was drawn within less than eight hours after onset of the attack. In 8 patients the first sample was obtained within twenty-four hours after onset. In 20 patients the first sample was obtained between the second and the eighth day after onset of acute symptoms. In 1 man, the first blood was drawn on the seventeenth day of illness; and in 1, on the twenty-first day.

Fasting blood samples were obtained repeatedly during the hospital stay. The smallest number of specimens obtained from a single patient was 9, and the greatest was 16. The last blood letting was performed in 1 instance after only ten days; and in 4 cases on the thirteenth, seventeenth and nineteenth day of acute illness, respectively. In 25 patients the last sample was taken between the twenty-first and thirty-fifth days. From 1 patient the last blood was obtained forty-two days after onset of infarction.

One man was a Negro. There were but 2 women in this series. The youngest patient was 47 years old and the oldest was 73 years. The average age was 57 years.

Five patients had had a prior episode of infarction. One had been stricken four years previously, 3 had had attacks two years previously, and 1 woman had had an attack only five weeks previously. One man had had two preceding attacks, three and two years before. Only 1 of the 30 patients had diabetes mellitus. Two patients had chronic nephritis and 1 had liver damage. One man had nephritis and liver disease.

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The oldest patient, who had diabetes mellitus and had had a previous attack of myocardial infarction four years before, died on the thirty-fifth day of illness; the last blood sample was withdrawn only seven and a half hours before death. Two much younger patients died a few weeks after discharge from the hospital.

Three patients experienced a second episode of infarction or extension of infarction during their hospital stay, manifested clinically and by electrocardiograms.

Results of serum studies in 30 patients with acute myocardial infarction were compared with results of similar studies in 44 presumably healthy persons, 10 patients with hypertension but without infarction, and 8 patients without infarction but treated with dicoumarol for thrombophlebitis. Single, duplicate, or triplicate serum assays were also made on blood samples from over 200 patients with various diseases unrelated to myocardial infarction.

Each specimen of blood serum was subjected to paper electrophoresis. A sample containing 8 lambda of serum was applied to each of three Whatman No. 1 filter paper strips. Electrophoresis took place at 7–10°C. for fourteen hours, at 3.2 A and 110 V (DC), in a sodium barbital-sodium acetate buffer of pH 8.5 and 0.1. Bio Blue, Sudan Black, and the periodic acid-Schiff reaction were used to demonstrate fractions of proteins, protein-bound lipids, and protein-bound carbohydrates, respectively (1, 2, 3). Total protein was assayed by the biuret method, total lipid by Bloor's method, and total cholesterol by the Schoenheimer-Sperry technic.

OBSERVATIONS

To facilitate analysis of patients' elpherograms, normal minimum and maximum values for the various serum fractions were arranged in Table 1. These "normal" values were arrived at under the described experimental conditions. These values might be normal and are being referred to as such. The term "healthy" should be substituted for "normal" with reference to the persons whose blood was used. There was a wide span between minimum and maximum values.

In patients with acute myocardial infarction, multiple and distinct deviations in elpherograms appeared simultaneously in an early phase of acute illness. Deviations were observed in the blood serum obtained within eight hours after onset of the attack. They were evident in half the blood samples studied within twenty-four hours, and in the remaining half they were apparent the next day. Changes were noted in all serum specimens tested within forty-eight hours after onset of infarction.

Proteidogram

In the patients with myocardial infarction, total serum protein levels ranged from 5.35 to 7.90 Gm. per 100 ml., and remained within normal limits throughout hospitalization. Only 1 patient had hypoproteinemia; this was due to severe hypoalbuminemia caused by severe albuminuria. In the healthy persons, minimum, average, and maximum serum albumin values were 2.05, 3.55, and 4.86 Gm. per 100 ml., respectively. Corresponding values for patients with infarction were 1.91, 2.53, and 3.65 Gm. per 100 ml. Only on the twenty-fifth day of illness were albumin levels usually within normal limits, though the maximum was still only 3.91 Gm. versus 4.86 Gm. for the controls. Since the concentration of total protein was normal, there was an increase in globulin reciprocal to the

TABLE 1

Minimum and Maximum Values for Serum Fractions in Healthy Persons

	TP	A	G	α_1	α_2	β	γ	A + α_1	G − α_1
PROTEIDOGRAM*									
Minimum (Gm. %)	5.35	2.05	2.27	0.26	0.25	0.28	1.03	2.57	1.14
Maximum (Gm. %)	7.90	4.86	6.39	0.82	1.11	1.89	3.02	6.39	5.54
Mimimun (%)	100	30.8	39.5	4.2	3.4	6.1	10.5	38.7	34.6
Maximum (%)	100	60.5	69.2	11.9	15.3	25.9	30.0	65.4	61.3
								TL	TC
	$A\alpha_1$	α_2	β_{tr}	β_r	β_1	β_{tl}	β_{ul}	mg./100 ml.	
LIPIDOGRAM†									
Minimum (%)	0	0	0	0	12.4	0	0	360	71
Maximum (%)	27.3	10.0	56.8	43.6	43.6	50.0	10.5	860	265**
	$A\alpha$	α_1	α_2	β	γ				
GLUCIDOGRAM‡									
Minimum (%)	0	10.9	20.4	14.7	8.2				
Maximum (%)	20.6	32.0	36.4	32.4	32.8				

* TP = total protein; A = albumin; G = globulin; α_1 = alpha$_1$-; α_2 = α_2-; β = beta-; γ = gamma-globulin. A + α_1, G − α_1 are listed for correlation with chemical assays.

† $A\alpha_1$ = albumin/alpha$_1$-; α_2 = alpha$_2$-; β_{tr} = beta, trés rapid-; β_r = beta, rapid-; β_l = beta, lente-; β_{tl} = beta, trés lente-; β_{ul} = beta, ultra lente-lipoprotein. TL = total lipid; TC = total cholesterol.

** Three of the 44 healthy persons had cholesterol levels above 200 mg. per 100 ml. of serum.

‡ $A\alpha$ = albumin/alpha-; α_1 = alpha$_1$-; α_2 = alpha$_2$-; β = beta-; γ = gamma-glucoprotein. ($A\alpha$ in albumin position, α_1 in alpha$_1$ position, α_2 in alpha$_2$ position of the proteidogram; all three are alpha-glucoproteins)

decline in albumin. Alpha$_1$-globulin was increased only erratically and moderately. In all patients, there was a sharp increase in alpha$_2$-globulin. In contrast to normal minimum, average and maximum values of 0.25, 0.73 and 1.11 Gm. per 100 ml., or 3.4, 10.9 and 15.3 per cent of total protein, these values for patients' serum were 0.50, 1.03 and 1.33 Gm., or 8.5, 13.8 and 20.3 per cent. Elevation of the alpha$_2$-globulin level persisted throughout hospitalization, although a tendency to adjustment was apparent from the twenty-second day of illness on. A tendency toward higher levels of beta-globulin was apparent in the increased minimum and average values; the maximum values were the same as in the controls. The frequency of two or three subfractions of beta-globulin was the same in the infarction patients as in healthy persons. The gamma-globulin level was increased only in patients with liver damage. Although increases in the concentration of alpha$_2$-globulin were the major factor in hyperglobulinemia, the changes in alpha$_1$-globulin and beta-globulin also contributed.

Lipidogram

Fluctuations of total lipid levels from person to person and in one and the same individual from day to day were of such magnitude that analysis of the data was useless. Similar oscillations of lipids were noted in both healthy and ill persons. On admission, the blood cholesterol level of all but 1 patient was within normal limits. One man was admitted on the eighth day of illness and his hemocholesterol concentration was 288 mg. per 100 ml. The lowest, average and highest blood cholesterol values for patients admitted within twenty-four hours after onset of infarction were 90, 162 and 202 mg. per 100 ml. of serum, respectively. In 3 patients of the series cholesterol levels had been determined from five to six months prior to infarction, and were 256, 280 and 300 mg. per 100 ml. The concentration of blood cholesterol rarely changed suddenly. In all patients who recovered, it increased; and in 3 patients who had a relapse during hospitalization, it declined. The blood cholesterol level of the patient who died on the thirty-fifth day of illness was 288 mg. per 100 ml. on admission (the eighth day of illness), 190 mg. on the seventeenth day, 265 mg. on the twenty-seventh day, 251 mg. on the thirty-third day, 170 mg. thirty-two hours before death, and 154 mg. per 100 ml. eight hours before death. Minimum, average and maximum cholesterol values on the day of discharge from the hospital, regardless of the length of time since the first day of illness, were 140, 201 and 265 mg. per 100 ml. Twelve of the 29 discharged patients had a hemocholesterol level exceeding 200 mg. per 100 ml.

The total amount of lipoprotein estimated from the total area of filter paper stained with Sudan Black was subject to the fluctuations of serum lipids and cholesterol. The difference from control serum pattern was not marked. Lipoprotein fractions were analyzed from various points of view. The frequency with which each fraction appeared was noted, the relative amount of each fraction was measured, and the numbers of fast, slow, and non-migrating fractions and the total number of all fractions were counted in the multiple blood samples from each patient. Results were not uniform and not significant. There was a downward trend of the first fraction (the albumin-alpha$_1$ peak) during the first ten days of acute illness, and then a gradual return to the normal height. The second peak corresponding to alpha$_2$-lipoprotein was usually absent on admission but, from the sixth or seventh day of illness on, such a peak appeared with increased frequency. The total amount of the two alpha$_2$-lipoprotein fractions was only slightly higher than in the controls. Fast migrating beta-lipoprotein fractions (β_{tr}, β_r) were rarely present on admission but, even after three days, nearly half of the patients showed such peaks. Later on, these rapid fractions were as common as in the serum of healthy persons. Slow migrating beta-lipoprotein fractions (β_1, β_{t1}) were just as frequent and just as large as in controls. The stationary beta-lipoprotein fraction (β_{u1}), rarely seen in healthy persons, was not uncommon in patients with acute myocardial infarction, especially in the second week of illness. This fraction was less frequently present after the twenty-second day of illness. Data on multiplicity of fractions could not be utilized. For several days, a single patient's serum might have but three beta-

lipoprotein fractions; then, for one day, five fractions might be present; from the following day on, again there might be only three fractions.

Glucidogram

Normally, the glucidogram has five fractions, of which the first three correspond to alpha-globulin, the fourth to beta-globulin, and the fifth to gamma-globulin. The first alpha-peak is in the albumin position in the proteidogram, the second is in the alpha$_1$-position, and the third in the alpha$_2$-globulin position. In patients with acute myocardial infarction, there is always a derangement of the glucidogram. The first (Aα) peak is usually decreased and often this fraction is absent. In 9 patients, it was missing at least once during observation, and in 1 patient it was absent from 6 of 16 blood samples studied. The second alpha-glucoprotein (α_1) had a tendency to increase, though the normal maximum of 32.0 per cent was rarely exceeded. In 1 patient, this fraction was elevated throughout the first eighteen days of illness: it was 38.2 per cent of total glucoprotein on the sixth day, 39.7 per cent on the seventh day, 34 per cent on the eighteenth day, 27.0 per cent on the nineteenth day, and 22.2 per cent on the twenty-eighth day. The third peak (α_2) was elevated in 28 of the 30 patients studied. One of the 2 patients without an increase in alpha$_2$-glucoprotein showed an increased in alpha$_1$-glucoprotein; the other showed an increase in gamma-glucoprotein. Considering normal minimum, average and maximum values as 20.4, 32.6 and 36.4 per cent, it was noteworthy that in all but 2 patients with myocardial infarction, these three values were higher. Within forty-eight hours after the onset of illness, minimum, average and maximum values for alpha$_2$-glucoprotein were 36.6, 40.8, and 45.7 per cent, respectively. Twenty-one patients had a value in excess of 40 per cent. The maximum figure (52.0 per cent) was observed in the diabetic patients who died. This value was obtained on the nineteenth day of illness; but thirty-two hours before death it was 43.0 per cent, and eight hours before death it was 39.2 per cent—still elevated, but at the lowest point during the entire observation period. Beta-glucoprotein did not deviate from normal. Gamma-globulin was increased in only a single patient. A maximum of 32.8 per cent was considered normal for this fraction. One man with marked nephrosclerosis and albuminuria showed, from the seventh day until the twenty-eight day of acute illness, a gamma-glucoprotein value which rose from 38.7 to 47.6 per cent; yet, on the thirty-fifth day of illness it was found to be 13.9 per cent of total glucoprotein.

DISCUSSION

In comparison with the elpherograms of healthy persons, the elpherograms of patients with acute myocardial infarction differ markedly. The proteidogram is characterized by hypoalbuminemia and hyperglobulinemia, the latter caused by a large and constant increase in alpha$_2$-globulin and by a moderate and inconstant increase in alpha$_1$-globulin and beta-globulin. The increase in alpha$_2$-globulin reflects the rise in alpha$_2$-glucoprotein; the increases in alpha$_1$-globulin and beta-globulin can be similarly explained. The increase in beta-globulin might

also be due to an increase in the beta-lipoprotein fractions. The decline in albumin is due to a decrease in albumin-alpha-lipoprotein and in the rapid alpha-glucoprotein fraction.

The serum lipidogram of patients with acute myocardial infarction is characterized regularly by a decline in the cholesterol level; a frequent decrease in alpha-lipoprotein fractions which migrate rapidly (albumin-alpha$_1$-) and an increase in those which move slowly (alpha$_2$-); a frequent decrease in rapid (beta, trés rapid; beta, rapid), and an increase in slow (beta, lente; beta, trés lente) beta-liproprotein fractions; and the frequent appearance of stationary (beta, ultra lente) beta-lipoproteins.

The glucidogram is characterized by a regular marked increase in alpha$_2$-glucoprotein. Occasionally, either alpha$_1$- or gamma-glucoprotein is increased instead of the alpha$_2$-fraction. The first, *i.e.*, the most rapid alpha- fraction (Aα), is decreased or absent, whereas the alpha$_1$-fraction is somewhat elevated.

All changes develop simultaneously but do not disappear at the same rate. By and large, deviations develop within the first forty-eight hours of acute illness, and frequently earlier. In 4 of the 30 patients of the series, electrophoretic alterations preceded electrocardiographic changes by from twenty-four to seventy-two hours. Often, multiple cardiographic tracings were needed to confirm the diagnostic impression gained from electrophoretic studies. During the course of illness there was excellent correlation with cardiograms. Thus, extension of infarction was reported independently by the two methods. Similarly, regression of blood alterations and reversal of clinical findings toward recovery were reported simultaneously and independently. Localization of myocardial damage as determined by electrocardiograms could not be correlated with the elpherogram findings. Correlation with the blood sedimentation rate failed utterly. The sedimentation rate was usually altered much later than the serum elpherograms. Changes in the glucidogram were unrelated to the sedimentation rate. In 1 patient, alpha$_2$-glucoprotein on one day was 42.8 per cent and on another day, 35.4 per cent; but on the same dates, the blood sedimentation rates were 19 mm. and 22 mm. per hour, respectively. There was no relationship to the prothrombin time. This is in direct contradiction to reports by others (4, 5). Elpherograms were not influenced by dicoumarol therapy, regardless of whether or not the patients had myocardial infarction or phlebitis. No conclusions could be drawn as to the possible relationship between blood pressure readings and elpherograms in our patients. Serum of patients having hypertension without acute myocardial infarction did not show the electrophoretic changes observed in the serum of patients with infarction.

With clinical regression of the acute illness, electrophoretic patterns tended to revert toward normal limits. The serum albumin level began to rise on the twenty-fifth day, and the globulin level started to decline. Alpha$_2$-globulin began to decrease from the twenty-second day on. Blood cholesterol concentration usually started upward after twenty-five days. Changes in lipoproteins generally lasted only twenty days. Elevation of alpha$_2$-glucoprotein was the most persistent feature, though high-normal values were often observed from the

third week of illness on, and were noted as early as twelve days after the onset of infarction.

Electrophoretic serum studies in patients with acute myocardial infarction have been reported only sporadically. Protein-bound carbohydrates generally have been neglected. Raynaud and co-workers studied protein fractions in 8 patients, 4 with recent infarction; 1 had angina, 3 had old infarction and angina, and 1 had angina pectoris without infarction (5, 6, 7). They concluded that a decreased alpha-globulin, increased beta-globulin, and normal gamma-globulin represent the typical pattern for atherosclerosis. Our observations are at variance with those of Raynaud *et al.* Malmros and Swahn (8) stated that beta-lipoprotein is increased in patients with myocardial infarction, even if the blood cholesterol level is normal. Gottfried and co-workers (9) studied lipidograms in 8 patients with acute myocardial infarction and compared them with 39 normal patterns. In 6 patients beta-lipoproteins were increased and gradually became adjusted to normal, in 1 patient they remained normal, and in 1 they increased on the twenty-sixth day only. These authors reported lability of lipoproteins. Levels of blood lipids, cholesterol, or both were increased in 60 per cent of patients with coronary disease.

Electrophoretic deviations, although dramatic are not diagnostic of acute myocardial infarction, unless supported by clinical data. Hypoalbuminemia accompanies innumerable diseases. Reversal of the albumin-globulin ratio occurs frequently. Hypocholesteremia develops in many debilitating conditions. Many reports are available on the increase of alpha$_2$-glucoprotein in various disorders (10). The combination of all the deviations observed in our series is less likely to occur in diseases other than acute myocardial infarction. Supported by clinical information and the exclusion of other diseases, the results of triple elpherograms gain considerably in diagnostic value.

Paper electrophoresis is a sensitive method. One might argue about the diagnostic value of the procedure but can hardly dispute the prognostic value of repeated assays. A progressive increase in alpha$_2$-glucoprotein and a decrease or disappearance of the first alpha-glucoprotein fraction, a progressive decline in the cholesterol level, a persistence of shift from alpha- to beta-lipoprotein and a decline of the stationary (chylomicron) beta-lipoprotein fraction indicate a poor prognosis. On the other hand, changes toward normal values, and a rise in the level of blood cholesterol are prognostically good. The elpherogram is not diagnostic per se, but is a diagnostic aid. Repeated assays are of greater value than a single determination.

SUMMARY

1. Repeated serum proteidograms, lipidograms, and glucidograms were obtained after onset of acute myocardial infarction and during hospitalization of 30 patients.

2. Regularly observed deviations were hypoalbuminemia, hyperglobulinemia, and an increase in alpha$_2$-globulin and in alpha$_2$-glucoprotein. Blood cholesterol concentration was lower during the acute illness than before or after. An in-

crease in alpha$_1$-globulin and beta-globulin, a shift from rapid to slow beta-lipoproteins, a decrease in the first alpha-glucoprotein fraction and an increase in the second, were frequent.

3. All deviations appeared within the first forty-eight hours after onset of infarction; the earliest positive findings were noted eight hours after onset. With recovery, deviations gradually disappeared (usually from the twenty-first day on), but not at the same rate. Aggravation of the deviations was indicative of extension of infarction.

4. Electrophoretic deviations closely paralleled clinical and electrocardiographic findings.

5. Changes in the proteidogram reflect changes in the lipidogram and glucidogram.

6. Simultaneous fractionation of proteins, protein-bound lipids, and protein-bound carbohydrates has diagnostic value and, if repeated, prognostic value in patients with acute myocardial infarction.

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MORBIDITY AND MORTALITY IN OLD AGE. A STUDY OF EXPERIENCE IN A MODERN HOME FOR THE AGED. PART IV*

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METHODS AND BASIC DATA (Continued)

Psychiatric Morbidity

The total study of psychiatric morbidity at the Home is composed of the following individual studies: The prevalence of mental disease at the Home on July 1, 1952; a comparison of prevalence of mental disease at the Home with that in published reports; probability of a resident of the Home being sent to a mental hospital; transfers to mental hospitals by nativity; and a comparison of the type of mental disorder requiring discharge from the Home, with that observed in first admissions to state mental hospitals in the United States.

Sources of data

Data for the study of the experience of those former residents of the Home who were sent to mental institutions between 1935 and 1951 were obtained from the "closed" records of the Home and a master table was constructed. The following items were included in the table: name, sex, date of admission, age on admission, marital status, nativity and number of years in the United States prior to admission, admission diagnosis, date transferred, reason for transfer, and where transferred. From the data obtained, it was possible to construct Table 150 (Part V)[1] which shows the cause for psychiatric discharge, by sex and by nativity, for the total period of this study.

The prevalence of mental disease at the Home on July 1, 1952

The prevalence of mental disease at the Home was calculated by dividing the number of active cases of mental disease by the population on July 1, 1952. The differences in prevalence rates were compared for significance, by sex, by determining the standard error of the difference (Table 54).

This number of cases of mental disease without doubt represented a minimum value, since in an unknown number of residents mental disease was present but was not detected because these persons never requested treatment or were not referred for psychiatric care.

From the files of the Psychiatric Department of the Home, it was determined that of the patients treated during the period January 1, 1951, to December 1,

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This study was carried out under the auspices of the Medical Services of the Home for Aged and Infirm Hebrews, New York, N. Y.

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[1] To be published, *J. Am. Geriatrics Soc.* October 1956.

TABLE 54

Internal Comparison of the Prevalence of Mental Disorders at the Home by Sex, on July 1, 1952

	Number with Diagnosis of Mental Disease	Number Without Diagnosis of Mental Disease	Total	Rate per 1000
Males	46	284	330	139.4
Females	107	476	583	183.5
Total	*153*	*760*	*913*	*167.6*

$$\text{S.E.}_{\text{diff.}} = \sqrt{\frac{(832.4 \times (167.6)}{330} + \frac{(832.4) \times (167.6)}{583}}$$

$$= \sqrt{662} = 25.75$$

$$\text{Dev}/\sigma = \frac{44.1}{25.75} = 1.71$$

1953, there were 381 who were still residents of the Home. The records of all 381 patients were studied. In addition to the standard admission data previously described, information was obtained relative to the date and reason for referral to the psychiatric department, action taken, and result of the action taken. All data were abstracted and recorded in a master table. From the completed master table it was possible to construct Tables 148 and 149 (Part V)[1] which show the various mental disorders diagnosed for these 381 patients, by sex and by nativity.

Comparison of the prevalence rate for mental disorders at the Home with the prevalence rates for mental disease in the Eastern District of Baltimore and Williamson County, Tennessee

Surveys of the prevalence of mental disease in the Eastern Health District of Baltimore (92) and in Williamson County, Tennessee (93) were used for comparison with the experience of the Home. These two surveys, although yielding valuable information for the communities studied, have many basic differences which make it extremely difficult to compare results. The demography of the two communities varied widely; important differences existed as to case finding methods and as to definitions of what constituted a 'case'; prevalence was computed differently in each survey; and different techniques and methods of classification were used. In both surveys no cases were examined by the survey staff psychiatrist, whereas every diagnosis at the Home was made by competent psychiatrists who examined and interviewed every patient at least once before arriving at a diagnosis. Also, undoubtedly, technics and methods of classification used at the Home differed greatly from those used in the other two surveys. However, since no other comparable data exist, comparison had to be made with the surveys in Baltimore and Williamson County or not at all. Statistical significance was determined by application of the following normal curve formula for comparison of a sample with a universe:

$$\frac{\text{Dev}}{\sigma} = \frac{q - q'}{\sigma q}$$

in which the q is the prevalence rate of mental disease in the Home, and q' the

TABLE 55

Comparison of the Prevalence of Mental Disorder at the Home with the Prevalence of Mental Disease in the Eastern District of Baltimore

Prevalence at the Home	= 167.6 per 1,000
Prevalence in the Eastern Health District	= 60.5 per 1,000

$$\sigma_{p_1} = \sqrt{\frac{(60.5 \times (939.5)}{913}} = 7.9$$

$$\text{Dev}/\sigma = 107.1/7.9 = 13.6$$

TABLE 56

Prevalence at the Home	= 167.6 per 1,000
Prevalence in Williamson County	= 69.4 per 1,000

$$\sigma_{p_1} = \sqrt{\frac{(69.4) \times (930.6)}{913}} = 8.41$$

$$\text{Dev}/\sigma = 98.20/8.41 = 11.68$$

prevalence rate of mental disease for either the Eastern Health District of Baltimore or the prevalence rate in Williamson County.[2] The value σq was obtained by the formula: $\sigma^2 q = \frac{p'q'}{N}$, in which N stands for the number of individuals present in the Home on the date in question (July 1, 1952).

Probability of a resident of the Home being sent to a mental institution

The probability of a resident of the Home being sent to a mental hospital during the period 1935 to 1951 was determined by life table methods in the following way. The discharge rates were derived by dividing the total number of discharges for psychiatric reasons for each sex during each time-period by the total age-specific-person-years of experience for the time-period for each sex (Tables 57–58). Thus, 19 males aged 60 and over were sent to mental hospitals during the six-year interval 1935 to 1940 (Table 59). For the same time-interval, the sum of the l_x values for males 60 and over was 952 (Table 57). Therefore, the rate of discharge for mental disease for males during this period was 19/952 X 1,000 or 19.93 per thousand person-years. Rates were determined for both sexes and for each time-interval. Male and female discharge rates were investigated to determine whether any trends existed in the probability of being discharged for mental causes over the three time-periods of the study, 1935–1940, 1941–1945 and 1946–1951. Comparison was by the chi-square test of association[3], with d.f. = 2. Comparison was also made between male and female discharge rates. Significance was tested by determining the standard error of the difference, and then by calculating the relative deviate[4].

[2] *Cf.* Tables 55 and 56.
[3] *Cf.* Tables 60–63.
[4] *Cf.* Table 64.

TABLE 57

Method of Obtaining the Annual Probability of Dying of Male Residents of the Home for Aged and Infirm Hebrews during Three Time-Periods since 1935

Age$_x$	1935–1940			1941–1945			1946–1951		
	l_x*	d_x†	1000 q_x‡	l_x	d_x	1000 q_x	l_x	d_x	1000 q_x
64§	53.75	5	93.02	35.25	4	113.48	40.00	1	25.00
69	207.25	25	110.97	70.75	10	141.34	91.75	4	43.60
74	318.25	40	125.68	235.00	34	144.68	232.75	31	133.19
79	214.50	30	181.82	178.25	42	235.62	367.25	62	168.82
84	105.50	25	236.97	75.00	25	333.33	235.50	54	231.26
89	42.75	16	374.27	47.50	17	357.89	83.75	25	298.51
94	10.00	4	409.00	9.25	4	432.43	28.00	11	392.86

* l_x = Total person-years in age group.

† d_x = Deaths in age group.

‡ 1000 $q_x = d_x/l_x$ = The probability of a person age x dying within the interval x to $x + 1$ (annual mortality).

§ Age 64 applies to all individuals from age 60 up to, but not including age 65. Age 69 applies to those from age 65 up to, but not including age 70, and so forth. Since the average age of the population in each five-year age group is not known, a very conservative estimate is taken, it being assumed that the average age is at the highest end of the scale.

TABLE 58

Method of Obtaining the Annual Probability of Dying of Female Residents of the Home for Aged and Infirm Hebrews during Three Time-Periods since 1935

Age$_x$	1935–1940			1941–1945			1946–1951		
	l_x*	d_x†	1000 q_x‡	l_x	d_x	1000 q_x	l_x	d_x	1000 q_x
64§	47.50	6	126.32	39.50	3	75.95	51.00	2	39.22
69	152.00	16	105.26	101.00	13	128.71	203.75	11	53.98
74	220.00	26	118.18	201.75	25	123.91	336.75	34	100.96
79	196.75	33	167.72	202.75	37	182.49	410.25	63	153.56
84	88.00	22	250.00	143.75	35	243.47	324.75	54	166.28
89	42.00	11	261.90	38.00	13	342.11	128.25	29	226.12
94	14.00	4	285.71	19.00	7	368.42	36.00	10	227.78

* l_x = Total person-years in age group.

† d_x = Deaths in age group.

‡ 1000 $q_x = d_x/l_x$ = The probability of a person age x dying within the interval x to $x + 1$ (annual mortality).

§ Age 64 applies to all individuals from age 60 up to, but not including, age 65. Age 69 applies to all those from age 65 up to, but not including age 70, and so forth. Since the average age of the population in each five-year age group is not known, a very conservative estimate is taken, it being assumed that the average age is at the highest end of the scale.

Transfers to a mental hospital, classified according to nativity

Comparison was made of the number of patients transferred to mental institutions during the time-interval 1935 to 1951, by nativity, in the following manner. Over the total period of this study, the native-born population of the

TABLE 59

Probability of a Resident of the Home for Aged and Infirm Hebrews Being Sent to a Mental Institution, 1935–1951

Year	Number Sent Out	l_x	Probability of being sent out (per 1000)
	MALES		
1935–1940	19	952*	19.93
1941–1945	17	651	26.11
1946–1951	11	1079	10.20
Total	47	2682	17.52
	FEMALES		
1935–1940	25	760.25†	32.80
1941–1945	10	745.75	13.40
1946–1951	16	1490.75	10.70
Total	51	2996.75	17.02

* Table 57, l_x column.
† Table 58, l_x column.

Comparison of the Probabilities of Being Sent to a Mental Institution for Residents of the Home for Aged and Infirm Hebrews, 1935–1951, by Time-Period

FEMALE RESIDENTS

TABLE 60. f Table

Year	Sent Out	Not Sent Out	Total	1000 q_x
1935–1940	25	735.25	760.25*	32.80
1941–1945	10	235.75	745.75	13.40
1946–1951	16	1474.75	1490.75	10.70
Total	51	2945.75	2996.75	17.02

$q_0 = 51/2996.75 = 17.02$ per thousand
* *See* Table 58, l_x column.

TABLE 61. f' Table

1935–1940	12.94	747.31	760.25	17.02
1941–1945	12.70	733.05	745.75	17.02
1946–1951	25.36	1465.39	1490.75	17.02
Total	51.00	2945.75	2996.75	17.02

$x/760.25 = 17.02 = 12.94$ per thousand

Home constituted, on the average, 20 per cent, and the foreign-born 80 per cent of the total population studies. The actual numbers of native-born and foreign-born who were discharged for psychiatric reasons were considered the observed (f) frequencies. By assuming that the native-born and foreign-born residents

Comparison of the Probabilities of Being Sent to a Mental Institution for Residents of the Home for Aged and Infirm Hebrews, 1935–1951, by Time-Period

FEMALE RESIDENTS

TABLE 62. $(f - f')$ Table

Year	Sent Out	Not Sent Out	Total
1935–1940	+12.06	−12.06	0
1941–1945	−2.68	+2.68	0
1946–1951	−9.34	+9.34	0
Total	0	0	0

TABLE 63. $(f - f')^2/f'$ Table

1935–1940	11.239	0.195
1940–1945	0.566	0.010
1946–1951	3.440	0.060

Degrees of freedom = $(r - 1) \times (c - 1) = (2) \times (1) = 2$.
$X^2 = 11.239 + 0.566 + 3.440 + 0.195 + 0.010 + 0.060 = 15.510$
$P < .01$

TABLE 64

Illustration of the Method of Comparison of the Probabilities of Residents of the Home for Aged and Infirm Hebrews Being Discharged to a Mental Institution, 1935 to 1951, by Sex

	Sent Out	Not Sent Out	Total	Rate per 1,000
Males	47	2635.00	2682.00	17.52
Females	51	2945.75	2996.75	17.02
Total	98	5580.75	5678.75	17.25

$$\text{S.E.}_{\text{diff.}} = \sqrt{\frac{17.25 \times 982.75}{2682} + \frac{17.25 \times 982.75}{2996.75}} = 3.46$$

$$\text{Dev}/\sigma = \frac{1752 - 17.02}{3.46} = 0.14$$

$P > .05$

TABLE 65

Observed Number of Native-Born and Foreign-Born Residents Sent to Mental Institutions Compared with the Expected Number, by Nativity, Assuming a 20 Per Cent Discharge Rate for the Native-Born and an 80 Per Cent Discharge Rate for the Foreign-Born

	f	f'	$(f - f')^2/f'$
Native-born sent to mental institutions	23	19.40	0.67
Foreign-born sent to mental institutions	75	78.60	0.16
Total	98	98.00	$X^2 = 0.73$

$\text{Dev}/\sigma = \sqrt{0.73} = 0.85$
$P > .05$

should have been discharged to mental hospitals in the ratio of 20 to 80, the theoretical frequencies (f′) were obtained. Comparison was by chi-square test[5] with d.f. = 1.

Comparison of type of mental disorder requiring discharge from the Home with that observed in first admissions to State mental institutions in the United States

During the period 1935–1951, residents of the Home were sent to mental hospitals, with one of six psychiatric diagnoses (Table 150, Part V)[1]. Most of the 98 residents had been sent out with a diagnosis in some category of chronic brain syndrome. It was planned to compare the number of residents according to psychiatric diagnosis with the number of patients with similar diagnoses admitted to state mental hospitals in the United States for the first time in 1948. However, it was not possible to make comparisons by application of the chi-square test of the goodness of fit or the normal curve, because most of the theoretical frequencies were less than 1. Therefore, the only comparison made was that between the number of discharged residents having the diagnosis of chronic brain syndrome and the number of subjects having such a diagnosis among first admissions to state mental institutions in the United States in 1948. The chi-square test of the goodness of fit, with d.f. = 1, was employed in the following manner[6].

The number of residents discharged with the diagnosis of chronic brain syndrome was the observed frequency (f), and the theoretical frequency (f′) was obtained as follows:

The admission rate to state mental institutions for patients aged 65 to 69 years with the diagnosis of chronic brain syndrome (all categories) was 99.6, and that for patients aged 70 and over was 258.9 per 100,000 civilian population (94). The estimated civilian population of the United States, aged 65 to 69 years, was 4,347,000 in 1948 (95). The estimated civilian population of the United States, 70 and over, was 6,601,000 in 1948. The estimated number of patients with chronic brain syndrome in the age group 65 to 69 who were admitted to state mental institutions in the United States in 1948 was $\frac{4,347,000}{100,000} \times 99.6$, or 4,333. The estimated number of patients aged 70 and over similarly admitted was $\frac{6,601,000}{100,000} \times 258.9$, or 17,087. Therefore, it is estimated that 21,420 patients, aged 65 years and over were admitted to state mental institutions in 1948 with a diagnosis in any category of chronic brain syndrome. In 1948 there were 24,577 admissions to the state mental hospitals of the United States of patients in age groups 65 and over, with all possible psychiatric diagnoses. Thus, it would be expected that $\frac{21,420}{24,577}$ or 87.2 per cent of 98 patients

[5] *Cf.* Table 65.
[6] *Cf.* Table 66.

TABLE 66

Number of Former Residents of the Home for Aged and Infirm Hebrews Admitted to State Mental Hospitals with Diagnosis of Chronic Brain Syndrome Compared with the Expected Number of Such Admissions, Assuming a Rate of 87 Per Cent

	f	f'	$(f-f')^2/f'$
Chronic brain syndrome, of all categories	71	85.41	2.43
All other disorders	27	12.59	16.49
Total	98	98.00	$X^2 = 18.92$

$\text{Dev}/\sigma = \sqrt{18.92} = 4.33$

admitted to mental institutions from the Home would have chronic brain syndrome; 87 per cent of 98 = 85.4 (f').

Mortality

The life table

Method of construction. Using the data obtained in the reconstruction of the population by entries and withdrawals, life tables were constructed. In the calculation of the basic element of the life table, nqx (the probability of dying within a stated interval), the direct method of allocating person-years of experience was used for the following reasons: 1) In all cases the dates of death and the year of entry into the Home were known and, for at least half the residents, the month of entry was also known. 2) The direct allocation method is the most accurate means of obtaining data on life-span studies. In this study, the individuals in the Home were followed over a number of years, whereas in the standard method a cross-sectional sample is taken at a given time and a theoretical set of values is constructed.

Certain basic rules for determining person-years were adopted:

1. Actual age is assumed to be one-half year older than stated age.
2. A person entering the Home is assumed to have entered on July 1 of the year of entry.
3. A person withdrawing alive in any year is assumed to have done so on July 1 of that year.
4. A person dying in any year is assumed to have died on December 31 of that year.

Thus, if the stated age on entry was 62, this is assumed to be 62.5. Age-specific death rates of the life table are different from those obtained from census and registration data. For age 60,

$$\text{the ordinary death rate} = \frac{\text{deaths at age 60}}{\text{population age 60}} \times 1{,}000,$$

but the average age of the population considered to be 60 is actually 60.5. The corresponding death rate in the life table, however, equals

$$\frac{\text{deaths at age 60}}{\text{population exactly age 60}}.$$

TABLE 67

Person-Years of Experience of John Doe, Aged 65, Who Entered the Home in 1936 and Withdrew Alive in 1946

Age Group	Time period		
	1935–1940	1941–1945	1946–1951
65–69	4.5		
70–74		5.0	
75–79			0.5

TABLE 68

Person-Years of Experience of Richard Roe, Aged 61, Who Entered the Home in 1935 and Died in 1949

Age Group	Time Period		
	1935–1940	1941–1945	1946–1951
60–64	3.5		
65–69	2.0	3.0	
70–74		2.0	3.0
75–79			1.0

Since the population aged 60.5 is smaller than that which is exactly age 60, the death rates shown in the life table will be smaller than the usual age-specific death rates. This difference is usually small, except in those age groups in which the risk of dying is considerable (60+, for example).

If entry into the Home occurred in 1938, the date of entry is assumed to have been July 1, 1938; and if withdrawal alive took place in 1938, it also is assumed to have been on July 1, 1938. Entry into the Home and withdrawal alive from the Home occur throughout the year, and each entrant and withdrawing resident is given credit for a half year of experience in the year in question as an average.

If death occurred in 1947, it is considered to have taken place on December 31, 1947. Each death receives credit for a full year of experience because the q_x value obtained by the direct allocation method must be made comparable to the q_x value obtained by standard life table methods. The following examples illustrate the application of these rules.

John Doe, aged 65, entered the Home for Aged and Infirm Hebrews in 1936 and withdrew alive in 1946. The person-years of experience in the Home in the three time-periods for which the probability of dying is being determined are derived in Table 67.

Richard Roe, aged 61, entered the Home in 1935 and died in 1949. His person-years of experience in the Home are calculated in Table 68.

By applying this procedure to every resident of the Home since 1935, the population at risk in each age group, in terms of person-years of exposure to the risk of dying, was calculated and is recorded in Tables 57 and 58 in the columns

TABLE 69

Life-Table Mortality Rates for Residents of the Home for Aged and Infirm Hebrews, 1935–1951

Age	1000 q_x	
	Male	Female
64	77.52	79.71
69	105.47	87.57
74	133.59	112.06
79	188.16	164.24
84	250.00	199.41
89	333.33	254.50
94	402.12	304.34

headed l_x. The number of deaths which occurred among the residents of the Home, by age and time-period, is recorded in the d_x columns. The probability of dying was calculated by the application of the formula, $q_x = \frac{d_x}{l_x}$, and is recorded in the 1000 q_x columns. The q_x's for the entire period 1935–1951 were obtained in much the same fashion (Table 69).

Method of construction of life tables for the Home. The q_x values obtained on the basis of the Home's experience from 1935 to 1951 represented the probability of dying before reaching the next birthday of a group of individuals with a five-year spread in age. The average age of these individuals was not known. In order to adopt the most conservative approach in the interpretation of these life-table values, that is, in order to place the experience of the Home in the most favorable light, it was assumed that the average age in each five-year age group was at the upper end of the span. Thus, the value for 60–64 was assumed to apply to age 64, that for 65–69 to age 69, and so forth. Age-specific death rates for men and women for each age from 60 to 94 were then estimated by interpolation or extrapolation. These basic values were used to construct life tables after the manner described by Greville (96).

United States life-table values. The q_x values for the United States for the years 1939–1941 were obtained from official sources (96). The q_x values for the United States for 1950 were obtained from the Actuarial Division of the Metropolitan Life Insurance Company of New York City. These values for 1950 were given for both sexes for each year of age, up to and including age 84 and for ages 89, and 94. The values for ages 85 to 88 and 90 to 93 were obtained by linear interpolation. Life tables were constructed and survivorship curves were drawn. The l_x values needed for the survivorship curves are shown in Table 70. They were derived in the following manner: the l_x value for age 60 was arbitrarily considered to be 100,000. A cumulative-distribution polygon (cumulative-percentage polygon, or curve) as described in Dixon and Massey (97) was constructed. For white males aged 60, the l_x value obtained from the United States life table,

1939–1941, was 67,721. For age 65, the l_x value from the United States life table was 58,215. Therefore, on the basis of an arbitrary value of 100,000 for age 60, the value for age 65 was $100{,}000 \times \frac{58{,}215}{67{,}721}$ or 85,962. All other values were derived as ratios of 100,000, the ratio being determined by the age-specific l_x value in the original United States life table. This process was repeated for each quinquennial year until age 95 for both sexes, and the results are shown in Table 70.

Comparison of q_x values for residents of the Home by time-period

The age-specific q_x values for both sexes were compared by time-period to determine whether any trends in the probability of dying existed for the residents

TABLE 70

United States l_x Values, Starting with a Cohort of 100,000 at Age 60

Age	Males		Females	
	1935–1941	1950	1939–1941	1950
60	100,000	100,000	100,000	100,000
65	85,962	86,940	90,118	92,312
70	68,802	70,989	76,461	81,492
75	49,083	53,580	58,423	66,111
80	29,120	33,717	37,685	46,963
85	13,089	17,771	18,773	27,782
90	4,004	7,623	6,474	13,404
95	782	2,593	1,415	5,172

Illustration of Method of Comparing Probability of Dying, for Three Time-Periods, by Age Group

COMPARING q_x FOR MALES, AGE 60–64

TABLE 71. *f* Table

Year	Died*	Survived	Total†	1000 q_x
1935–1940	5	48.75	53.75	93.02
1941–1945	4	31.25	35.25	113.48
1946–1951	1	39.00	40.00	25.00
Total.....	10	119.00	129.00	77.50

q_0 = 77.50 (per 1000) = 10/129

TABLE 72. *f'* Table

1935–1940	4.17‡	49.58	53.75	77.5
1941–1945	2.73	32.52	35.25	77.5
1946–1951	3.10	36.90	40.00	77.5
Total.....	10	119	129	77.5

* *See* Table 57, d_x column

† *See* Table 57, l_x column

‡ $X/53.75 = 77.5 = 4.165$

Comparison of Probability of Dying, for Three-Time Periods, by Age Group

COMPARING q_x FOR MALES, AGE 60–64

TABLE 73. $(f - f')$ Table

Year	Died	Survived	Total
1935–1940	+0.83	−0.83	0
1941–1945	+1.27	−1.27	0
1946–1951	−2.10	+2.10	0
Total	0	0	0

TABLE 74. $(f - f')$ $2/f'$ Table

1935–1940	0.6889/4.17 = 0.165	0.6889/49.58 = 0.014
1941–1945	1.613/2.73 = 0.591	1.613/32.52 = 0.50
1946–1951	4.41/3.10 = 1.423	4.41/36.90 = 0.120

Degrees of freedom = $(r - 1) \times (c - 1) = (2) \times (1) = 2$

$X^2 = 0.165 + 0.14 + 0.591 + 0.500 + 1.423 + 0.120 = 2.363$

Computation of Critical Ratios of Differences in q_x's between Residents of the Home for Aged and Infirm Hebrews and the White Population of the United States in 1939–41 and 1950

TABLE 75

Example

Females, the Home, age 69, $q_x = 87.75$; $n = 456.75$

Females, the United States, 1939–41, age 69, $q_x = 38.74$

$$\sigma_{p_1} = \sqrt{\frac{.03874 \times .9613}{456.75}} = .00905$$

$\text{Dev}/\sigma = .0489/.00905 = 5.40$

TABLE 76

Example

Females, the Home, age 69, $q_x = 87.75$; $n = 456.75$

Females, the United States, 1950, age 69, $q_x = 29.85$

$$\sigma_{p_1} = \sqrt{\frac{.0299 \times .9701}{456.75}} = .0079$$

$\text{Dev}/\sigma = .0577/.0079 = 7.30$

of the Home during the total period of this study. The significance of difference was tested by employing the chi-square test of association[7], d.f. = 2. Only those values for P which were 1 per cent or less were considered significant.

Since no significant differences were observed in the q_x values for the three time-intervals, life tables were constructed for the period 1935–1951, using all the available data. The q_x values needed for these life tables were derived by dividing the total number of age- and sex-specific deaths during the period 1935–1951 by the total age- and sex-specific person-years of experience (Tables 57 and 58).

Comparison of Home and United States q_x values

The 1935–1951 q_x values for the residents of the Home were compared by age and by sex with the corresponding q_x values for the white population of the

[7] *Cf.* Tables 71–74.

United States in 1939–1941 and in 1950.[8] Statistical significance was determined by application of the following normal-curve formula for comparison of a sample with a universe: $\frac{\text{Dev}}{\sigma} = \frac{q - q'}{\sigma q}$, in which q is the life-table mortality for the Home and q' the life-table mortality for the United States; σq was obtained by the formula $\sigma^2 q = \frac{p'q'}{N}$, in which N stands for the number of person-years of experience in the Home. Any Dev/σ of 2.58 or more (P = 1 per cent or less) was considered to be statistically significant.

(To be continued)

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CLINICAL USE OF THE BENDER VISUAL MOTOR TEST IN PSYCHOLOGIC ASSESSMENT OF THE AGED

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To meet the need for more objective and precise evaluation of the relative personality integration of the aged, professionally qualified psychologists, utilizing various established testing procedures are being called upon increasingly. The various aspects of the function of the psychologist who specializes in this field, especially in institutional settings, have been described in detail by Klopfer (1).

Problems which arise in connection with the interpretation and use of test data gathered in this extreme area of the age range are, however, far from definitive solution. For one thing, there are few normative data on performance in this group. For another, differences in cultural background among the aged, and associated linguistic and educational factors, make interpretation and cross comparison of relative integration very difficult. Moreover, theories which have evolved in relation to the tests have yet to take into full account the special problems of the aged with respect to the study of personality and integrated functioning.

A procedure which holds considerable promise as a means of swift evaluation of the psychologic status of the aged person, with special emphasis on degree of overall integration, is the Bender visual motor test. Its practical advantages, especially in institutional settings, are its brevity, ease and simplicity of administration, innocuous appearance to the subject, and its relative freedom from cultural influences. We shall consider in greater detail its structure and relevant aspects of its theoretical background, and we shall illustrate its utility by means of case abstracts. The particular cases discussed are drawn from among the residents of a home for the aged and reflect problems which confront the personnel of administrative and medical staffs. In a broader sense, they are representative of varying degrees of integration among aged persons.

The Bender-Gestalt test, as it is more commonly known, consists of nine designs constructed by Wertheimer and selected by Bender. (They are commercially available from the American Orthopsychiatric Association. Only these standard designs may be used as test stimuli.) Copies of the actual test designs are reproduced in the following sections. The method of administration is based upon recommendations by Hutt (2) and is the one utilized by the present writer.

TEST MATERIALS AND ADMINISTRATION

The required equipment is minimal. It consists of the following: the test designs (each on a separate card), blank unruled paper 8½ by 11 inches in size, a medium soft pencil, and an eraser.

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Before the test starts, the examiner should have his materials in readiness. The cards should be arranged in correct order and placed upon the table, face down. A sheet of blank paper should be placed upon the table in front of the subject, along with the pencil and eraser.

When the subject enters, the first steps will involve getting rapport. Some examiners may prefer using the Bender-Gestalt test as a buffer when other tests

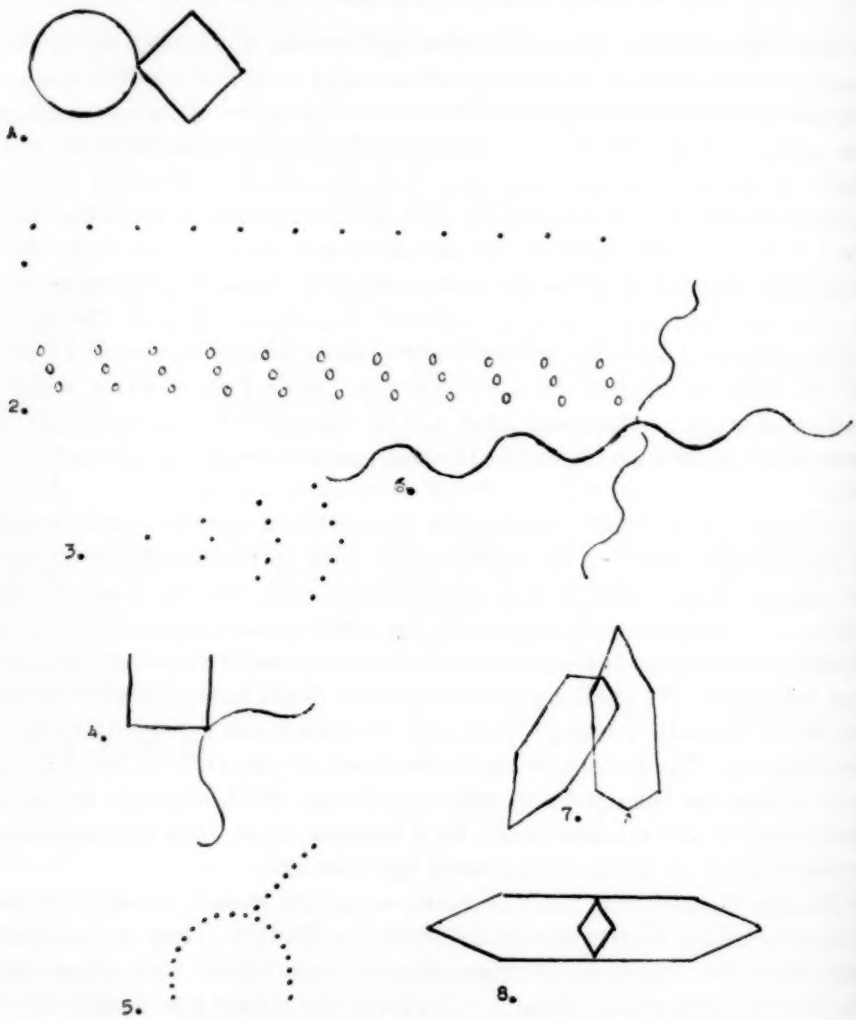

FIG. 1. Designs of the Bender-Gestalt test.

are to be administered, because its non-emotionally charged content and its non-verbal character may be suitable as a starting point. Others may prefer inserting this test in the middle or at the end of the total series of tests. In any case, it is highly important that the subject be given a suitable orientation to the task and that he accept it as a necessary part of the testing situation. It is essential that his cooperation be obtained. The techniques which the examiner may employ in gaining these ends will vary with the individual subject and with the situation.

The examiner says: "I am going to show you some cards, one at a time. Each

card contains some simple designs. I would like you to copy these designs on paper as well as you can. Work in any way that is best for you. This is not a test of artistic ability, but copy the designs as well as you are able to."

The examiner then presents card A with the base (marked with the letter) toward the subject, and says, "Copy this as well as you can." The subject is not permitted to use any mechanical guides. All cards are presented in the same way. If the subject is unable to complete the task on one sheet of paper, additional paper may be given him. Only one card is exposed at a time. All questions the subject may ask (such as amount of time to be used, corrections or erasures, placement of the designs on the paper, or the size of the reproductions) are referred back to the subject for his decision, with the remark, "Do it the way you think best," or "That's up to you," or "There are no rules about the way you can work." This is regarded as most important, since it is one of the fundamental assumptions of this test procedure that the unique manner in which the subject organizes and plans for the test situation will reveal essential aspects of his personality organization and processes.

THEORETICAL CONSIDERATIONS

The response of the individual to the stimulus designs is discussed by Bender (3) as a "gestalt function" defined as "that function of the integrated organism whereby it responds to a given constellation of stimuli as a whole." It is considered that the whole setting of the stimulus and the whole integrative state of the organism determine the pattern of the response. There is a tendency for the individual to reorganize the stimulus changes in accordance with principles which may be determined by his sensory motor pattern of action. This pattern of action may be expected to vary in different maturation levels and in pathologic states. With increasing damage to the cortex, for example, there seems to be a lessening of the capacity to copy the designs, resulting in primitivation of forms and in destruction of the patterns of forms. Thus, the perception and reproduction of the stimulus designs among the aged will be primarily dependent upon biologic characteristics associated with the integrative integrity of the functioning nervous system.

The role played by maturation, illustrated by Bender's investigation of children's drawings, is of secondary importance in the present paper. Also of secondary significance are factors of disorganization associated with functional disturbances. We shall not go into the presumed psychosexual symbolic valences of the stimulus designs. We are here primarily concerned with changes in the quality of reproduction of the designs associated with possible nervous-system deterioration or disease which result in a psychologic deficit in the aged. It should be pointed out that little has been carried out in the way of systematic study of the effects of aging *per se*, in this connection. Suggestive evidence is contained in the work of Stainbrook and Lowenbach (4), Pascal and Suttell (5), Schilder (6), and Orenstein and Schilder (7). All of these investigators used the test to evaluate disintegrative and reintegrative changes in the course of convulsive and other disorganizing treatments of the nervous system. Schilder, using the test immediately after insulin reaction and after Metrazol convulsion, found the following

features in reproductions of the stimuli: perservation, substitution of circles and loops for points or dots, curves for angles, rotations, and separation within the individual designs. Evidence cited by Pascal and Suttell (5) suggests that such features may be characteristic of senile individuals.

The foregoing findings and empirical observations by this writer suggest that the test may be used to evaluate differential impairment of essential aspects of psychologic functioning. These aspects, considered as ego functions (5), may involve such features as sense of self, orientation in time and space, regard for reality, and the capacity for thoughtful consideration. Since our prime concern is with the overall integration of the gerile individual, it is apparent that the technique is of the greatest relevance. From a practical point of view, in homes for the aged, such as those to which the writer acts as consultant, assessment of this area is of critical importance. In the emphasis upon interdependent group living, considerable demand is placed upon the individual for a comparatively high level of self reliance. Comprehension, the ability to act upon instruction, personal orientation in time and space are all essential attributes of personality for living in situational settings in which it is anticipated that the resident will remain ambulatory and continue to participate in community affairs. Thus it becomes necessary to obtain a measure of the individual's effective integration in order that screening, activity planning, or therapeutic programs may be carried out. The Bender-Gestalt may serve this purpose.

Although, in general, manifestations during the test will vary in accordance with the nature and extent of the damage, most important evidence of impairment among the aged will be reflected in:

1. Partial rotations of designs.
2. Exclamations of impotence, perplexity, and incompetence (including professions of inability to complete task).
3. Marked perservation of dots or lines.
4. Loss of detail.
5. Fragmentation.
6. Difficulty with acute angles.
7. Overlapping of the designs.

Extremes of such manifestations, especially when there are several types represented, probably indicate a cortical pathologic condition in the aged subject. Beyond this, however, the performance of the gerile person may be interpreted with regard to such important considerations as the likelihood of successful adjustment in the specific setting involved. It has been pointed out that the relative integration of the individual as measured by the test may provide an objective basis upon which to plan activities, initiate a therapeutically oriented regimen, or consider alternate placement. Moreover, test results may be interpreted and utilized to convey an appreciation of the aged person's problems in this area to interested and involved staff personnel, and this may lead to the establishment of differential expectancies, in terms of activity, upon a more realistic basis.

Quantitative methods. An early standardization of the test for children was undertaken by Bender. Subsequently, a scoring system was developed by Pascal

and Suttell for use with adults. Unfortunately, the use of this system with gerile subjects must be discouraged. For one thing, the method was standardized on a population ranging in age from 15 to 50, an area in which factors of aging are not important determinants of performance. For another, this system too greatly penalizes the gerile subjects for the tremor which is common to old age. The evolution of an acceptable quantitative method for the elderly population is to be desired. Nevertheless, aspects of performance which may never be part of a quantitative analysis are important variables for consideration and interpretation by the clinician. The subject's mode of working, his attitudes toward the task, his attitudes toward being examined, his relationship with the examiner, and the degree of concentration he manifests—all of these factors must be integrated with the objective results in order to yield meaningful psychologic assessment.

CLINICAL ILLUSTRATIONS

The following case material, illustrative of the test in psychologic assessment of the aged, is interpreted in the light of the empirical observations of the writer as well as upon the basis of evolving theory and previous studies concerned with its application in this area. The observed relationships between the test performance and the behavior of the subject are reported as suggestive evidence which should be subjected to further investigation among various groups of the aged.

A 69-year-old man had come to the Home from a rented-room situation in which he was no longer able to care for himself. He had been ill for a long time. Immediately following admission, he seemed to alternate between symptoms of agitated depression, walking back and forth in the halls berating his own fate and that of other residents, weeping when spoken to sympathetically, and having a challenging "chip on the shoulder" attitude toward other residents and administrative personnel. In an interview he revealed great concern about being properly fed and about his bowel problems. When examined psychologically, he wept and said, "I came here too soon; I'm too young for this place." (As judged by the average age, approximately 79, he was not altogether wrong.) The reason for referral was the desirability of psychologic assessment, in view of his disturbing behavior following admission and the suspicion on the part of the staff that his apparent irrationality might reflect pathologic substrata of personality. Interviews had revealed considerable affective volatility and some poorly disguised aggressive feelings. Therefore, staff concern about the integration retained by this individual gained greater prominence. His reproductions of the Bender designs are seen in Figure 2. Data from the Bender-Gestalt and other tests did not indicate serious pathologic trends or psychologic deficit. Important for our present discussion, however, is a review of the evidence concerning the degree of effective integration which is revealed in this person's drawings. For example, it may be noted that this man was sharply and clearly aware of his environment (the good, clear forms) and could comprehend and act upon instructions. There was less motor difficulty than is characteristic of most other residents of the Home. Also to be carefully noted are his elaborations and painstaking corrections of designs, which revealed that he was capable of self-criticism and was aware of his own errors. The lack of perseverations in designs 2, 3, 4 and 6, and the ability to maintain the angularity in designs A, 5, 7 and 8 indicated a level of integration which was far above the lapse into the rounding of the angles which is typical of the drawings of both senile adults and immature children.

Rounding of angles by the senile aged, being a primitivation of form, is considered to be associated with behavioral regression. This report of relative inte-

gration was borne out by later improved adjustment and full-scale participation in occupational therapy projects and in community life, following the initial psychologic trauma of adjustment.

Figure 3 shows the test designs drawn by a man who was referred for psychologic assessment in order to determine his suitability as a candidate for admission to the Home. This man, aged 72, was neatly dressed and was accompanied by his daughter. He was reluctant to speak with the examiner and seemed to be looking to his daughter for guidance. When left alone with the examiner, he managed to obstruct questioning or examination by repeatedly stating that he had excellent references, citing names of individuals who would vouch for him and speaking at length of his synagogue affiliations. He said, "I'm sure I can make good here; if I don't, you just put me out." Actually his adeptness at parrying made it difficult to assess the degree of integration from interview or from verbal tests. He seemed to regard the examination as threatening, and would not deviate from his pattern of non-cooperation. Finally the Bender-Gestalt test was utilized, because of its innocuous non-verbal character. The results revealed the extreme degree of impairment in this individual.

It should be noted how the initial design A reflects this person's seeming abilities when observed on a fairly superficial level. It is a less than adequate reproduction, but it does reflect the almost successful facade which the man presented. The trauma to the nervous system is clearly revealed, however, in the markedly poor utilization of space which resulted in complete disorder of the design placement, the inability to discriminate between forms, and in the perseverative drawing in all designs in which dots or loops are involved. These aspects of the drawings plus the subject's tendency to be unable to distinguish between various parts of the same design reflected his confusions in relation to the external environment. Reversals and rotations, as shown in designs 5 and 6, further illustrate the internal chaos which accounted for his gross disorientation.

Following administration of the test, frank discussion with this applicant's daughter revealed that he had been forgetful in the extreme and very disoriented, even in his own home. It was then possible to refer her to the social worker, who pointed out the futility of attempting to integrate her father within the Home, where the orientation demands were beyond his capacities, and urged upon her the consideration of alternative placement where he could be given the close nursing supervision obviously required.

Frequently, changes in behavior serve as warnings to staff personnel that internal changes are taking place in the aged person. Without knowledge of the etiology, degree, and transient or permanent quality of the changes, little can be done to make the individual more comfortable and to effect appropriate modifications of his activities or daily regimen. Sometimes there is no great certainty as to whether the changes in the individual are functional or organic in nature. Here again the test may be of aid in specification of the nature of the changes and of their dimensions.

A female resident, 87 years of age, had been admitted three years previous to examination. At that time she had been regarded as an average admittee, in good physical and mental health. She was viewed as capable of active participation in most of the activities for residents. Hence it was puzzling to the staff that she did not involve herself in other than eating, sleeping and "sitting for hours on end." Thus, far from living up to expectations in terms of a degree of activity, this woman simply "vegetated." Despite her age, her appearance betokened good health, and this was confirmed in physical examinations. Evidence of this health, such as her excellent appetite and sound sleep, made her non-par-

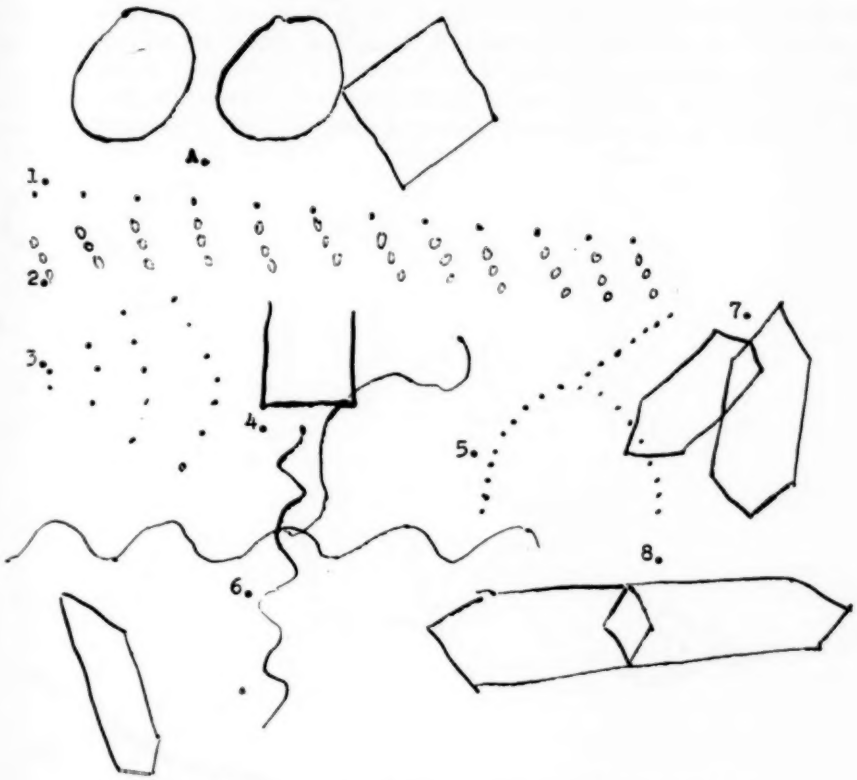

FIG. 2. Test figure reproduction by 69-year-old new resident.

ticipation all the more frustrating to well intentioned staff members. Bender-Gestalt evaluation, however, gave some indication of the determining internal state of affairs (Fig. 4).

The primitivation of percept of form is well illustrated by this individual's reproductions of the test designs. The total inability to deal with angularity suggested a psychologic regressiveness which eliminated the possibility of thoughtful consideration of thought or action. The preserved discreteness of the designs reflects her retained ability to maintain such automatic or conditioned behaviors as are involved in meeting meal-time schedules or in other basic and rudimentary aspects of living. Her arbitrary divisions of design 1 suggest that she had settled on certain modes of response which she deemed adequate and that there was an inability to go beyond this level. Spontaneity was no longer possible for this person. The fragmentation and discontinuity in almost all her copies of the designs reflected her inability to make sense out of her environment. On the other hand, the impotence she experienced was revealed by the failure to carry through to a conclusion on most of the designs, as well as by her frequent verbalizations of "What do you wish from me? I can't do this."

In this case, it was important to obtain this assessment so that staff personnel who came in contact with this resident would be aware of her limitations. Thus, they would not rely upon external appearances alone in planning her activities and in their own expectations of her.

The following illustration shows the relationships between behavioral changes occurring over a period of time in one aged person and the reflection of those changes in the test results.

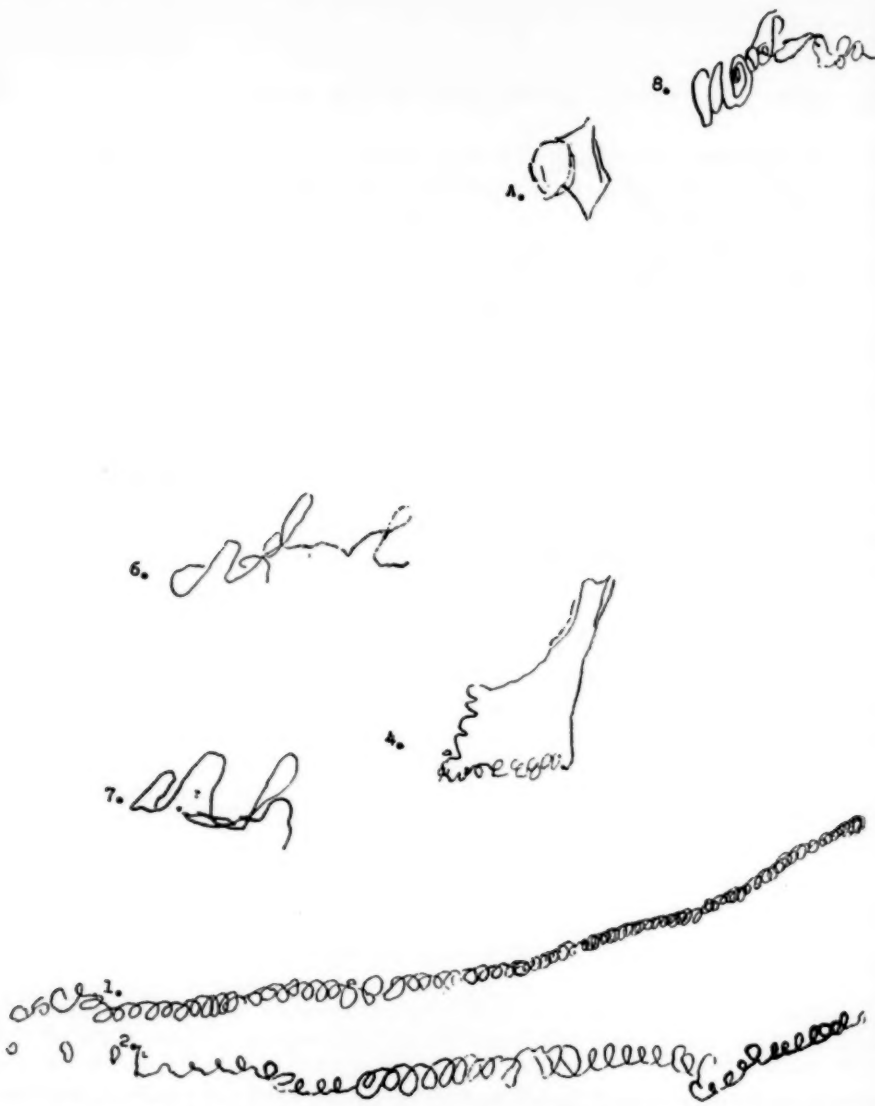

FIG. 3. Test figure reproduction by 72-year-old applicant for admission.

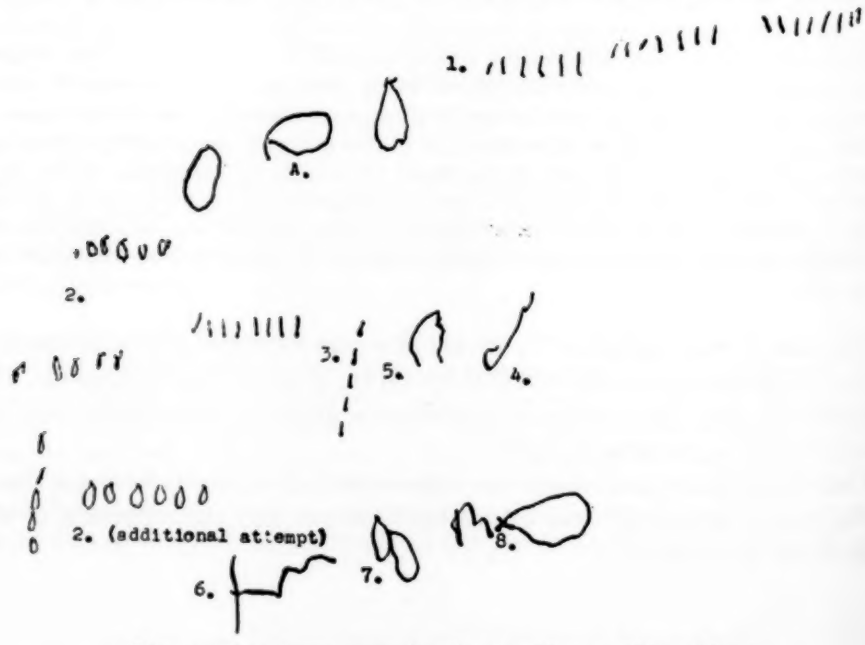

FIG. 4. Test figure reproduction by 87-year-old resident.

An 84-year-old female resident had been referred for examination as part of a general psychologic survey of the Home population. She had been described to the writer as an active participant in community affairs, and as a modest, unassuming woman who impressed others with her pleasant manner and disposition. She was held by staff personnel to be a model of "preservation" and was regarded, in many ways, as an ideal resident.

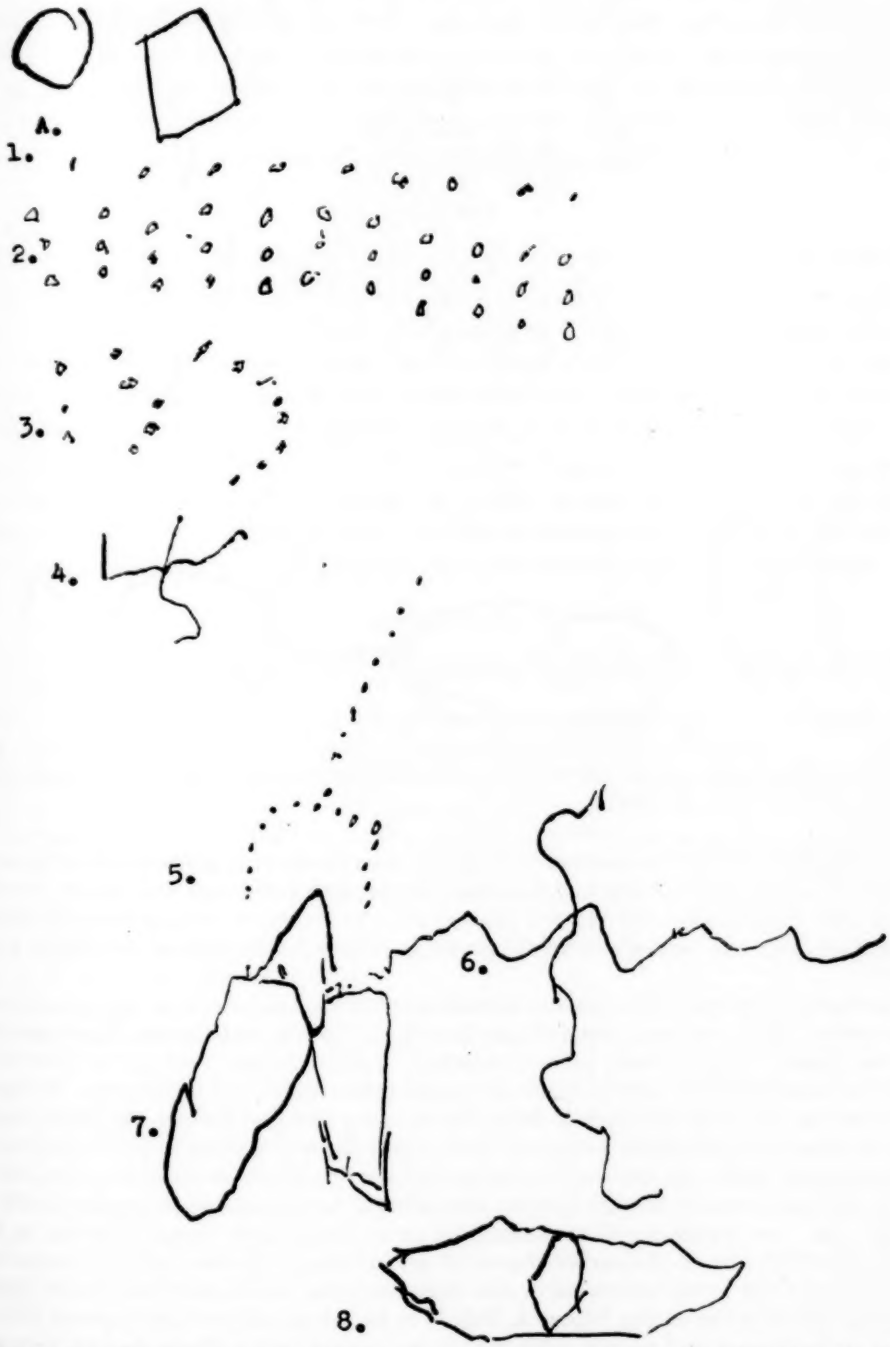

FIG. 5. Test figure reproduction by 84-year-old resident prior to deterioration involving behavioral changes.

FIG. 6. Test figure reproduction by 84-year-old resident following sudden deterioration involving behavioral changes.

Six months later she was re-examined. In the interim she had, in the words of the social worker, "slipped badly." She had become quite forgetful and was very much disturbed about this. Emotionally, she showed signs of greatly increased unhappiness and unusual irritability. Her test reproductions are shown in Figure 5 (the earlier) and Figure 6 (the later).

Comparison between the reproductions obtained in the earlier and in the later examinations reveals the loss of control which was involved in the internal changes. Such angularity as this woman was previously able to maintain in her drawings vanished in favor of the spheroid construction so characteristic of a more primitive level of integration. In Figure 6 the structure of design 3 is seen to have lost its curvature and become rigidified, whereas that of design 4 became fluid. Designs 1 and 2 reveal hitherto lacking perseverative tendencies distinctly unlike the more or less controlled and effectively directed loops and dots of the earlier performance. Design 5 shows almost total destruction when compared with the earlier copy, and design 6 suffers similarly in great degree. Only design 4 retains at least some approximation to the earlier degree of organization. Another point of comparison, and an aspect not to be overlooked by the clinician, is the heaviness of the line in Figure 6 as compared with the earlier Figure 5. This is to be taken into account together with the lesser tentativeness and tremor exhibited in the second series. These factors were asso-

ciated with the behavioral manifestations of increased irritability and carelessness manifested by this formerly very mild and cooperative individual.

In these case illustrations we have attempted to provide, through utilization of an objective measure in the hands of the clinical psychologist, a means of assessment and of understanding of the psychologic status of the aged person, in terms of effective integration. Prognostically, appraisal of present status and of changes by the Bender test has significance in indicating probable behavioral developments. Also, the test results may be utilized in relation to the equally important aspect of gaining comprehension and appreciation of processes involved, on the part of staff or nursing personnel who deal with the aged.

SUMMARY

The utilization of the Bender visual motor test as a method of assessment of relative integration among the aged is discussed. A description of the test and details of administrative procedures are presented. The theoretical assumptions upon which the test is based and the empirical results obtained by its use in groups of individuals with known impairment or disorganization of cortical processes suggest that it is eminently suitable for such assessment of aged persons. The utility of the test in an institutional setting is demonstrated by means of presentation of case material in which the ability of aged individuals to reproduce designs is compared with their behavior. The practical significance of the test as an economical method of psychologic evaluation of the aged is emphasized.

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DERMATOSES IN THE AGED*

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In order to discuss the dermatoses of persons in the older age group, it is necessary to establish the onset of old age. From a cutaneous point of view, it begins when the deterioration of the skin exceeds its generation—usually between the ages of 40 and 45 years. When degenerative changes overbalance regenerative processes, the ultimate dermatosis is known as senile atrophy. Its onset is influenced by many factors including heredity, general health, skin care, disease, and undue exposure to the elements. Under these influences, skin age may vary considerably with chronologic age.

The more common geriatric dermatoses are divided into four major groups in order to simplify their presentation:

Physiopathologic conditions.
Metabolic conditions.
Cardiovascular conditions.
Miscellaneous disorders.

DERMATOSES ASSOCIATED WITH PHYSIOPATHOLOGIC CHANGES

Senile atrophy. Senile atrophic changes in the skin usually begin in the fourth decade of life. Histologically, the epidermis becomes thinner, and mitoses in the prickle and basal layers become more scarce. The papillae become flattened and lose their elastic fibers. The collagen fibers grow thinner, and the elastic fibers show clumping, thickening and irregular positions together with marked hyperplasia, especially in the face and neck. This hyperplasia may account for the yellowish tinge in the face and hands of some old people. The elastic fibers in the blood vessels, especially the elastica interna, participate in this change. The alterations in the elastic tissue seem to depend, to a large extent, upon exposure to sunlight and the elements, and are hastened by radiation. The sebaceous glands are generally reduced in number, except on the nose and forehead where hyperplasia of these structures is common after the age of 40 years. The subcutaneous fat shows degeneration. The water content of the skin is reduced. Insensible perspiration is diminished and, as a result, less water and sebaceous activity cause the dryness associated with senile atrophy. Capillary reactivity to mechanical and other stimuli becomes gradually slower, both in the response and in the return to normal status. Much of the pruritus in the elderly may be secondary to this vascular change.

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Senile atrophy cannot be remedied but the condition may often be postponed by protecting the skin from exposure to the sun and elements, by providing the skin with the best possible nutrition and hygiene, and by applying suitable emollients. Numerous reports have appeared in the literature during the past few years attesting to the efficacy of topical hormone preparations in the treatment of senile atrophy.

Senile pruritus. This distressing condition usually involves the trunk but is often generalized in distribution. It is probably due to a combination of factors related to atrophic and degenerative changes in the skin and vessels of the elderly patient. Cutaneous changes are limited to atrophy and secondary traumatic dermatitis. It is important to exclude lymphoblastomas, allergic conditions, hepatitis, diabetes, malignancy, and drug sensitivity in the differential diagnoses.

Treatment consists of the application of antipruritics and the maintenance of water and oil in the skin through the use of petrolatum or other greasy bases.

Pigmentations. Senile hyperpigmentations may begin between the ages of 40 and 50 years. These take the form of lentigines. They appear as blotchy brown and black spots and occur predominantly on exposed surfaces. Changes in hormonal balance at this age partially account for their appearance. Pigmented nevi already present frequently become darker and grow in the elderly. Keratoses also occur.

Cosmetically unattractive superficial pigmentations may be easily removed by peeling methods, such as the cautious application of trichloracetic acid or carbon-dioxide snow.

Seborrheic keratoses. These begin as small yellowish-to-brown areas that increase in size and thickness and become more deeply pigmented. Typically, they have a "stuck on" appearance. The surface is usually covered with a thin greasy scale, but not infrequently it is dry and verrucous. Unless secondarily infected, there is a lack of induration or inflammatory reaction. Seborrheic keratoses appear chiefly on the trunk and arms and less commonly on the face and neck. They are benign lesions and not precancerous.

Treatment consists of curettement and the application of a hemostatic agent such as Monsel's solution, or light desiccation.

Senile keratoses. Senile keratoses appear as firmly adherent dry crusts of yellowish-to-brown color. In contrast to seborrheic keratoses, they appear chiefly on exposed surfaces such as the temples, ears, neck and dorsa of the hands. If the adherent crust is removed, the under surface shows prolongations that match depressions on the underlying skin. Senile keratoses are precancerous lesions and may show some surrounding inflammatory reaction when undergoing malignant degeneration. If epitheliomas develop, they are of the prickle-cell type. These keratoses may also become cutaneous horns (cornu cutaneum).

Great care should be taken in the removal of senile keratoses. The areas should be well curetted and the base of the lesion well cauterized with a desiccating or coagulating current.

Leukoplakia vulvae. Leukoplakia may occur as a single entity or in association with kraurosis vulvae or lichen sclerosus et atrophicus. It frequently appears

during or shortly after the menopause. Leukoplakia is essentially a hypertrophic process manifest as discrete plaques, single or multiple, with a whitish or blue-gray color and thickening or accentuation of the normal lines of cleavage. The plaques may develop on the inner surface of the labia, clitoris, perineum or vaginal mucosa. Associated pruritus is a predominant symptom. This is a precancerous condition, and may progress to Bowenoid changes or prickle-cell epithelioma. The appearance of fissures or ulceration in leukoplakia is a strong indication of malignant change.

Treatment consists of the removal of irritating factors, that is, the treatment of any underlying condition. Local destructive measures may also be used, if the area of involvement is not widespread. Most important is clinical observation for the possibility of malignant change.

Kraurosis vulvae. The etiology of this sclerosing atrophy of mucocutaneous structures of the vulva is unknown. It presents a glistening whitish to reddish-blue surface. As the disease progresses, marked atrophy of all of the female genital structures occurs. It is often preceded by intense pruritus that may persist. There may be accompanying leukoplakia or neurodermatitis or both.

The administration of estrogenic substances by local, oral or parenteral routes may be of value. Some investigators have obtained good results with diathermy.

Basal-cell epithelioma. This condition begins as a discrete pinhead to pea-sized pearly nodule that gradually enlarges and finally ulcerates. The ulcer progresses slowly and has a raised pearly telangiectatic border; it may be superficial or deep. Basal-cell epitheliomas are of many varieties; among them are the morphea-like, cystic basal-cell, and pigmented basal-cell types. There are also mixed metatypical and intermediate metatypical types.

Squamous or prickle-cell epithelioma. These epitheliomas frequently develop on exposed surfaces in elderly persons, either in relation to, or independent of senile keratoses and senile cutaneous changes. Occasionally they are sequelae of precancerous chronic dermatoses. Practically all epitheliomas in the mucous membranes of the mouth, nasopharynx and genitalia are of the prickle-cell type. The most common site is the lower lip. Some lesions are characterized by a crateriform ulcer with a wide rolled and indurated border; not infrequently verrucous, papillomatous or fungoid lesions are seen. There are two primary clinical types: 1) the papillary superficial type that may or may not evolve from senile keratoses, leukoplakia or persistent cheilitis, and 2) the ulcerative infiltrative type. Those of the papillary type may remain locally malignant for a considerable period of time. Those of the ulcerative type can develop early metastases.

The treatment of basal-cell epithelioma consists of local destruction by chemosurgery, curettage, electrodesiccation, or excision that may or may not be followed by x-ray therapy. For prickle-cell epithelioma, wide excision of the lesion or adequate roentgen-ray therapy is necessary. Biopsy confirmation for diagnosis, type and extent of the lesion should be obtained prior to treatment.

Malignant melanoma. The most malignant and rapidly fatal of all cutaneous neoplasms is the malignant melanoma. Although it usually appears after the age of 50 years, it may occur at any age. Malignant melanomas may arise spontane-

ously, or from other types of pigmented nevi—the junction nevus being by far the most common. From 30 to 60 per cent of patients with this malignant lesion present clinical or anamnestic evidence of occurrence at the site of a pigmented nevus. A malignant melanoma usually begins as a blue-black nodule; occasionally, it is lighter in color or even nonpigmented. The change from a benign nevus is often noted by extension of pigment at the periphery and some evidence of an inflammatory process. The most common sites are the soles, palms and genitalia. Malignant melanoma is to be distinguished from the blue nevus, pigmented basal-cell epithelioma, ordinary nevi, seborrheic keratoses, small angioma, hematoma and granuloma pyogenicum.

Malignant melanoma should be treated surgically with wide local excision and regional node dissection.

Senile ectasias. These are small hempseed-sized bright red-to-purplish raised areas that consist of dilated capillaries. They occur mainly on the trunk and upper chest and are benign in nature.

Treatment by local destruction is for cosmetic purposes.

Acrochordon. The soft wart is a form of fibroma that occurs on the face and neck and between the shoulders, chiefly in elderly people. Pinhead to pea-sized soft pedunculated lesions appear, which leave empty wrinkled tags or sacs.

Treatment is for cosmetic purposes and consists of removal by simple excision at the base.

Senile sebaceous adenoma. Senile sebaceous adenomata appear as small, flat-topped, umbilicated papules usually located on the forehead. This condition is due to hypertrophy of the sebaceous glands, and is most common in those past middle life. The papules may appear in association with rosacea.

The condition is benign. Treatment is for cosmetic purposes, and consists of incision and expression of the contents.

DISEASES AND CONDITIONS SECONDARY TO METABOLIC CHANGES

Vitamin deficiencies. Although vitamin deficiencies occur in persons of all age groups, factors peculiar to old age alter the absorption and transportation of food and make elderly individuals more susceptible. Inadequate mastication because of loss of teeth, decreased secretion of digestion enzymes and hydrochloric acid by the stomach and intestinal tract, impaired gallbladder function interfering with fat utilization, atrophy of the intestinal mucosa impeding absorption, and diminished mucous secretion leading to impaction and constipation are factors that produce vitamin deficiencies in the geriatric patient. Many of these deficiencies are manifested by certain skin disorders. However, not all of the disturbances are clearly limited to the deficiency of a single vitamin.

Vitamin A plays an important part in the metabolism of epithelial structures, both of the skin and of mucous membranes. With deficiency of this vitamin, the skin appears dry and roughened and presents firm conical pigmented papules with spines projecting from the hair follicles. Night blindness is often associated with vitamin A deficiency. Localized keratoderma of the palms, soles, elbows and knees is thought to be due to lack of vitamin A. The Sjörgen syndrome, characterized

by marked dryness of all mucous membranes, and especially of the lacrimal and salivary glands as well as mucous glands of the respiratory tract, is seen most frequently in middle-aged women. According to some reports, it improves with massive vitamin A therapy.

Vitamin B_1 (thiamine) deficiency is concerned primarily with beriberi, in which edema of the skin may be the first sign. In many cases of pellagra, thiamine deficiency is also present.

A symptom complex produced by riboflavin (vitamin B_2) deficiency has been described. This consists of a macerated linear fissure at each angle of the mouth with a red scaly inflammation along the vermilion border of the lips. There may also be a mild seborrheic dermatitis-like eruption in the nasolabial folds and at the inner and outer canthi of the eyes. As with thiamine, riboflavin deficiency is often associated with pellagra. Some investigators think that the keratitis associated with rosacea may be a result of deficiency of this vitamin.

The most widely known of the deficiency disorders is pellagra, caused by a deficiency of nicotinic acid. The earliest skin lesions have the appearance of sunburn. The erythema proceeds to a reddish-brown color that desquamates. Bullae may develop in the subsequently edematous skin, and secondary infection is common. Regardless of type, the lesions are always well defined. After recurrent attacks, the skin becomes thickened, scaly, and pigmented. Lesions are found chiefly on exposed surfaces; symmetry is striking. Paresthesia of the buccal mucosa and burning sensations of the pharynx or esophagus frequently occur. The tongue often becomes swollen and presents a dry surface that bleeds easily; the tip and sides are reddened and smooth. Seasonal recurrences are common, usually beginning in the spring and subsiding during the winter months.

Vitamin C (ascorbic acid) deficiency causes scurvy, in which both skin and mucous-membrane lesions may be present. The gums are characteristically swollen and spongy, and bleed easily. Petechiae and ecchymoses appear first on the legs and then extend to the arms and trunk. Brawny tender swellings may develop from these extravasations, especially on the legs and abdominal wall.

In treating vitamin-deficiency disorders in the elderly patient, care must be taken to discover and treat any underlying contributory causes. Dietary deficiencies require supplementation in accordance with the patient's ability to eat. Vitamin therapy should be prescribed. The prevention of secondary infection and disease in the debilitated individual can be controlled by general supportive measures and the use of antibiotics.

Xanthelasma. Of the skin diseases due to faulty lipid metabolism, the only one specifically limited to the older age group is xanthelasma. The disease usually has its onset at middle age, and is most commonly found on the upper lid at the inner canthus. Asymptomatic lesions appear as yellowish plaques, pinhead to pea-size or larger. About 40 per cent of patients with xanthelasma have increased levels of serum cholesterol and total blood lipids. The association of cardiovascular disease is significantly frequent.

Xanthelasma may be treated by careful application of trichloracetic acid to the affected area, electrodesiccation, or surgical excision.

Keratoderma climactericum. Haxthausen described keratoderma climactericum in 1934 as a circumscribed hyperkeratosis, chiefly of the palms and soles, occurring at the menopause. It is accompanied by various signs and symptoms, among which are obesity, hypertension and arthritis. The hyperkeratosis is symmetrical and corresponds to areas exposed to pressure and friction. There is no erythema or subjective sensation of burning or itching. The disease is believed to be due to deficiency of estrogen and responds to treatment with estrogen and topical keratolytic medication.

SKIN DISEASES AND CONDITIONS SECONDARY TO CARDIOVASCULAR CHANGES

The skin is frequently a reflector of disturbances in the cardiovascular system. These disturbances increase in frequency with age. Consequently, skin disease secondary to cardiovascular change becomes a frequent disorder in the later decades of life. The skin manifestations are those of decreased blood supply, but they vary, depending upon whether the defect is arterial or venous. Common findings in cardiac decompensation are edema and occasional eczema of the lower legs. These signs disappear and reappear with corresponding changes in cardiac function. Arteriosclerosis affects the arteries of the skin as well as those of other organs. Clinical signs of this change are best observed on the feet. The skin becomes dry and the nails atrophic or thick. The hair over the dorsal area disappears. Wounds and infections are difficult to heal. As pruritus is often a feature, excoriations and secondary infections are common. That circulatory disturbances may cause similar manifestations on the hands is often overlooked.

By far the most common skin disease of vascular etiology in the older age groups is stasis dermatitis. This occurs in persons with edema of the legs, most frequently in association with varicose veins or a history of phlebitis. Lesions commonly appear on the inner aspect of the lower legs above the ankle. Initially, the skin appears cyanotic, erythematous and swollen. It later becomes eroded and ulcerated. Associated hyperpigmentation is often found. Stasis ulcers occur in devitalized sites usually around the malleoli. The ulcer margins are irregular and soft and the base infected. Autosensitization may cause eczematoid lesions to appear elsewhere on the body, particularly on the arms, trunk and thighs. This is frequently initiated by the application of topical medications to the area of stasis dermatitis.

The treatment of skin conditions in this group depends primarily upon improvement of the impaired circulation to the area involved. In arterial disase, vasodilation by medical or surgical means, specific exercises, and general skin care are the basis of treatment. In venous deficiency, elevation of the legs, elastic stockings, and Unna boots combined with bland topical medications and antibiotics will control most cases. Surgical stripping of veins is often a preventive as well as a therapeutic means of treating venous insufficiency.

MISCELLANEOUS DISORDERS

Exudative discoid and lichenoid chronic dermatosis. This chronic dermatosis usually appears in men during the fourth or fifth decade of life. It is charac-

terized by a generalized eruption with multiform lesions that may be exudative, lichenoid, or urticarial. The picture may resemble that of the premycotic stage of mycosis fungoides. The lesions occur in phases with partial remissions and exacerbations. All types may be present at once but usually the majority are of one particular phase. Severe pruritus is the most annoying symptom.

Treatment consists of carefully controlled steroid therapy. Arsenic orally and parenterally has also been effective.

Acne varioliformis. Acne of this type is a relatively rare disease, occurring predominantly in women in or near middle life. It is characterized by discrete and indolent reddish-brown papules and pustules that become covered with crusts and leave superficial scars on healing. The site of predilection is over the brow and scalp. It has been established that there is a microbic factor in the etiology, but gastrointestinal disorders are believed to have some causal relationship.

Treatment consists of topical applications of bactericidal preparations.

Angular stomatitis. Chronic resistant fissuring of the labial commissures is not infrequently found in elderly persons. This is a result of deepened folds at the corners of the mouth caused by the sagging of tissue and augmented by edentia or malocclusion from ill-fitting dentures. Pockets are formed where saliva collects and keeps the skin moist and macerated. The principal etiologic agent, which is probably bacterial or fungal, has a good medium for growth in the moist and macerated tissue.

Treatment is directed at the correction of dental malocclusion. Local antibiotics or fungicidal preparations are used.

Colloid milium. Colloid milium occurs on the face and the back of the hands in men and women, especially after the age of 45 years. It is characterized by groups of lemon-yellow elevations on the skin, the individual lesions ranging from pinhead to pea size. On puncture, a soft gelatinous mass may be extruded. The cause of colloid milium is not known, but vitamin C deficiency may be a factor.

Acrodermatitis chronica atrophicans and lichen sclerosus et atrophicus. Two atrophic skin diseases of unknown etiology occur predominantly in the later decades of life, and usually in women. Acrodermatitis chronica atrophicans primarily involves the extremities. It is a true atrophy of both the epidermis and the cutis, and appears as wrinkled skin, as thin as tissue paper, through which the deeper vessels are readily visible. The earliest changes appear as bluish-red infiltrations on the exterior surfaces, especially in relation to the joints. Slowly these resolve, leaving characteristic changes. The disease is usually bilateral, but cases with unilateral involvement do occur and may be confused with linear scleroderma. Although the etiology of this disease is unknown, the numerous reports on the efficacy of penicillin in the early stages indicate an infectious agent.

Lichen sclerosus et atrophicus usually appears on the upper portion of the trunk, the neck, axillae and forearms. The eruption is characterized by discrete or grouped flat-topped white papules that show comedone-like plugs on the smooth surface. The plugs are situated at the pilosebaceous or sweat-pore orifices. Atrophy occurs in the later stages, and the plugs then become more promi-

nent. Many cases involve the vulva and anal region. There is some confusion as to the distinction between this condition and kraurosis vulvae.

No method of treatment is satisfactory. Periods of remission and exacerbation may occur and occasionally lesions undergo spontaneous involution.

CONCLUSIONS

Older people are susceptible to the same skin diseases as younger people. In addition, they are more susceptible to a special group of dermatoses caused by disturbances peculiar to this age group—namely, the physiopathologic alterations in the skin, metabolic imbalances, cardiovascular changes, and miscellaneous disorders.

With the development of the newer corticosteroids and broad-spectrum antibiotics, the dermatologist has additional tools with which to treat skin diseases successfully in the older age group. These new drugs in many instances have been life-saving.

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Abstracts of Current Literature

TREATMENT OF CARDIAC ARREST AND SLOW VENTRICULAR RATES IN COMPLETE A-V HEART BLOCK. USE OF MOLAR AND HALF MOLAR SODIUM LACTATE: A CLINICAL STUDY.

Bellet, S.; Wasserman, F., and Brody, J. I. *Circulation* **11:** 685 (May) 1955.

After epinephrine, Neosynephrine, and atropine were without effect in restoring the ventricular beating during repeated, prolonged periods of ventricular standstill in a case of Stokes-Adams syndrome. Molar and half molar sodium lactate, administered intravenously, restored the heart beat on ten separate occasions. After two hours, the heart continued to beat spontaneously for several hours. In the case of terminal cardiac arrest, the intracardiac injection of sodium lactate temporarily restored ventricular beating. Sodium lactate was administered to 3 patients with complete A-V heart block. One patient presented a ventricular rate of 15 per minute, widened QRS complexes, and a state of shock. Sodium lactate increased the ventricular rate to 60 per minute and increased the blood pressure to 120–140 systolic with resultant marked improvement in the patient's clinical state. The widened QRS complexes were significantly narrowed. Decrease in the rate of administration or cessation of administration of the lactate solution on two separate occasions resulted in a return of the electrocardiographic ventricular rate to the control level of 15 per minute. After five hours of administration, the ventricular rate had increased to 60 per minute and was maintained without further lactate administration. About one hour later normal sinus rhythm was restored. In a second case of complete A-V heart block, the ventricular and atrial rates were significantly increased following the administration of sodium lactate. In a third case of complete A-V heart block, with occasional normally conducted beats, the complete A-V heart block was abolished and the idioventricular beats were entirely replaced by normally conducted beats. Sodium lactate appears to have marked qualities of increasing cardiac rhythmicity though possessing little or no pressor action. Observations in human beings and in experimental animals suggest that this solution possesses qualities that should be of help in the prevention and therapy of sudden cardiac standstill. In addition, it does not induce dangerous ectopic rhythms. The dose, method of administration, and fate of sodium lactate in the body are discussed. The possible mechanisms by which it produces the effects described are outlined. (From author's summary)

ARTERIOSCLEROTIC OCCLUSION OF CEREBRAL ARTERIES: MECHANISM AND THERAPEUTIC CONSIDERATIONS.

Bruetsch, W. L. *Circulation* **11:** 909 (June) 1955.

An attempt was made to elucidate the mechanism by which narrowing and occlusion of arteries occurs in arteriosclerotic softening of the brain. In an extensive histologic examination of 20 brains with arteriosclerotic encephalomalacia, no evidence of the occurrence of true thrombosis was observed. As the microscopic study progressed, emphasis shifted from the lipid deposit to the fibroblastic part of the atherosclerotic plaque as the major factor in the obliterative sclerosis. The presence of "embryonic foci of cellular proliferation" in the plaque appear to be the source for the slow extension of the fibroblastic obliteration in the large cerebral and other vessels, such as the coronary arteries. In the small cerebral arteries, occlusion is caused by endothelial proliferation. The proliferative changes of the endothelial cells in the small cerebral vessels, as well as the proliferation of the fibroblasts in the atherosclerotic plaques, is viewed as a morbid process occurring at a time in the individual's life when various cell types show great propensities for abnormal growth. (Author's summary)

CORTICOTROPIN (ACTH) IN HEART DISEASE: ITS PARADOXICAL EFFECT ON SODIUM EXCRETION IN RESISTANT CONGESTIVE FAILURE.

Camara, A. A., and Schemm, F. R. *Circulation* **11:** 702 (May) 1955.

A clinical trial of corticotropin was undertaken in hopeless and terminal cardiac patients with resistant edema. Of 21 patients (8 arteriosclerotic, 3 hypertensive, 8 chronic rheumatic, and 2 with cor pulmonale), 17 (81 per cent) were benefited by the hormone. The responses were as follows: 1) In 4 cases, spontaneous diuresis occurring *during* (usually the fourth to sixth day of treatment) and continuing after the course of corticotropin therapy with loss of previously resistant edema. 2) Spontaneous diuresis *after* discontinuation of corticotropin with edema weight loss and relief of intractable pulmonary passive congestion in 3 patients. 3) An altered response to mercurial diuretics in 10 patients previously refractory, responding effectively *during* or *after* corticotropin therapy. Of the 4 cases showing no improvement, 3 were chronic valvular disease on a rheumatic basis, and 1 was arteriosclerotic heart disease. The initial increase in edema with the use of corticotropin is minimized by the adjuvant use of a diuretic regimen which is reviewed in brief. Continued use of the same regimen after the course of corticotropin maintains and potentiates the beneficial effects of the hormone. Speculations on the possible mode of action of corticotropin, based on observations by the authors and studies of other investigators, led to the tentative conclusion that cortisone or some other still undiscovered adrenal hormone produced in response to corticotropin stimulation, may overcome by antagonistic action on the renal tubules the sodium-retaining effect of desoxycorticosterone-like substances which are also presumably produced by the adrenal cortex in response to corticotropin administration. The possibility remains, based on clinical observations, that corticotropin may, directly or through some other adrenocortical hormone, produce an improvement in the failing myocardium. (Excerpt of authors' summary)

NEOPLASTIC INVASION OF THE HEART AND PERICARDIUM.

Cohen, G. U.; Perry, T. M., and Evans, J. M. *Ann. Int. Med.* **42:** 1238 (June) 1955.

The literature on metastatic tumors of the heart and pericardium is partially reviewed and the pertinent clinical features described. In an analysis of 1,007 consecutive autopsies performed during a 57-month period, 65 tumors metastatic to the heart or pericardium, or both, were found among 315 malignant tumors of all kinds—an incidence of 20.6 per cent. Diagnosis was made prior to death in 3 patients and suggested in 2 others. Tumors of the breast, bronchus, the lymphoma group, and malignant melanoma accounted for about three fourths of the cases with cardiac metastasis. This is in agreement with the experience of others. The development of one or all of the triad of cardiac failure, cardiac arrhythmias or cardiac compression in patients known to have malignant disease should suggest the possibility of metastases to the heart or pericardium. From this and other recent studies, it would appear that neoplastic invasion of the heart is more frequent than was formerly believed, and should be given consideration in the differential diagnosis of heart disease. (Authors' summary and conclusions)

ELECTROCONVULSIVE THERAPY IN ELDERLY PATIENTS.

Ehrenberg, R., and Gullingsrud, M. J. O. *Am. J. Psychiat.* **111:** 743 (Apr.) 1955.

Mental illness in individuals over 65 years of age is not necessarily organic and irreversible. The so-called functional psychotic reactions in the elderly represent the response of the organism to the psychologic and physiologic stresses of aging. They are not the inevitable result of senile or arteriosclerotic brain changes. They may occur in the absence of significant intellectual deterioration. The most frequent psychotic reactions in the elderly are psychotic depressive reactions, manic depressive reactions, paranoid states, and schizophrenia-like conditions. These functional conditions in the elderly respond well to electroconvulsive therapy and the risk to an individual in a reasonable state of health is

minimal. Conventional electric shock therapy, unmodified by curare-like drugs was used in 112 patients 65 to 85 years of age at the Boston State Hospital during the years 1948 through 1953. The results are reviewed. As a result of this therapy, 78.5 per cent were able to leave the hospital and 55 per cent could remain out for longer than a year. Depressed patients showed significant improvement even after three treatments. Patients with paranoid or schizophrenia-like reactions required more treatments than depressed patients in order to obtain a remission. The schedule ultimately adopted was three treatments the first week, two the second week, and then one weekly. In this way, significant memory defects and confusion were usually avoided. Those that occurred were reversible and of short duration. One patient died as an immediate result of electroconvulsive treatment. The treatment may have contributed to delayed deaths in 3 others with severe physical illnesses. The life expectancy was poor before treatment and their physical condition rather than their age accounted for the outcome. Only 4 compression fractures of dorsal vertebrae occurred among 1,329 electroconvulsive treatments. It would appear that diminished muscle bulk in the elderly compensates for the seemingly increased risk of osteoporosis and makes the use of curare-like drugs unnecessary. Relapses occurred in 37.5 per cent of recovered patients but most of them again responded to treatment. More relapses occurred in the group who had had attacks of mental illness before age 65. More patients among those that never left the hospital had their first attack of mental illness at age 65 or over.

DIE BEDEUTUNG DER "PARADOXEN" HORMONBEHANDLUNG.

Englhardt-Gölkel, A. *Deutsche med. Wchnschr.* **80:** 712 (May 6) 1955.

Experience with androgen-estrogen therapy in 50 menopausal patients confirmed its favorable effect upon the general condition of the patient, the vasomotor disturbances, the backache, and the arthritic pains. Other indications for this therapy include hyperfunction of the thyroid during the menopause or preclimacteric changes, prevention of thyroid growth during thiouracil treatment, the side effects of ACTH or cortisone treatment, nephrosis, and certain types of renal disorders. In view of effects on the performance, for example, of the heart muscle, further therapeutic uses may be found for this combination of hormones.

AMYLOIDOSIS IN RHEUMATOID ARTHRITIS, AND SIGNIFICANCE OF "UNEXPLAINED" ALBUMINURIA. A REPORT OF EIGHT CASES.

Fearnley, G. R., and Lackner, R. *Brit. M. J.* **1:** 1129 (May 7) 1955.

Among 183 patients with rheumatoid arthritis examined during a one-year period, 8 were found also to have amyloidosis which is one of the few potentially fatal complications. It usually is not recognized during life. These patients were screened, using albuminuria as the clinical guide, since the essential morbidity of this complication is due to renal involvement. The modified Congo-red test of Unger and coworkers proved more reliable than the standard Congo-red test in establishing the diagnosis. In all 8 patients, the rheumatoid arthritis could account for the complication; in 1, pre-existing tuberculosis may have played a part. Inasmuch as conditions which in the past caused amyloid deposition are now largely controlled by chemotherapy, and since rheumatoid arthritis is extremely common, it may become the principal cause of amyloidosis.

FULMINANT NORMOCHOLESTEREMIC XANTHOMATOSIS (HISTIOCYTOSIS X).

Goldner, M. J., and Volk, B. W. *A. M. A. Arch. Int. Med.* **95:** 689 (May) 1955.

A review of the unified concept of the diseases of the reticulum-cell system is presented, according to which Hand-Schüller-Christian disease, Letterer-Siwe disease, and eosinophilic granuloma of bone are to be considered as different phases and different manifestations of a single nosologic entity and no longer as independent diseases. The concept is based on the functional interrelationship of the histologic lesions in these three conditions.

The new entity is called eosinophilic normocholesteremia xanthomatous granuloma or histiocytosis X. The disease is rare in adulthood and senescence, but with a better knowedge of the syndrome and wider use of diagnostic laboratory aids, particularly tissue biopsies, more adult cases are being recognized. The disease seems to occur predominantly in males, both among children and in adults. The clinical course and the postmortem findings in an instance of this disease in an elderly woman are presented. Evidence could be found of almost all features of the different phases which are characteristic for the gradual evolution of the lesions of the syndrome, and which are as follows: 1) A proliferative phase consisting predominantly of reticulum cells and histiocytes, with accumulation of eosinophils. 2) A granulomatous phase, with increase of blood vessels, fibroblasts, eosinophilic leucocytes, histiocytes, giant cells, and incipient lipid phagocytosis. 3) A xanthomatous phase in which aggregations of foam cells containing lipid-staining material become evident. 4) A fibrous phase, considered a healing stage, in which the granulomatous lesions are gradually replaced by connective tissue. As the etiology of the disease has not been established, no effective therapy is as yet available. The localized eosinophilic granuloma of bone may be self-limiting or accessible to surgery. Various procedures have been proposed for the disseminated acute or chronic forms. Antibiotics have been useful in a few instances and disappointing in others. Dietary management with restriction of cholesterol appears to be valueless. X-ray therapy seems to yield the best results. The reticulum cells seem to be most sensitive to radiation.

BLOOD VOLUME IN CONGESTIVE HEART FAILURE.

Gunton, R. W., and Paul, W. *J. Clin. Invest.* **34:** 879 (June) 1955.

Blood volume studies by the P^{32}-tagged red blood cell method have been made on 102 patients with congestive heart failure and on 107 control subjects. Patients in congestive heart failure usually have a larger blood volume than the controls. With compensation there is usually a decrease in blood volume, principally of its plasma fraction. With the spontaneous reappearance of congestive failure, the blood volume usually increases again. The etiologic type of heart disease and amount of edema do not determine the blood volume changes in heart failure, with the exception of pulmonary heart disease in which the red cell volume is high. In some cases of congestive heart failure, blood volume may be normal and may not decrease with compensation or increase with the reappearance of failure. (From authors' summary.)

STELLATE GANGLION INFILTRATION IN ORGANIC PSYCHOSES OF LATE LIFE.

Haber, J. *Am. J. Psychiat.* **111:** 751 (Apr.) 1955.

Stellate ganglion infiltration was performed in 8 patients, aged 48 to 76 years, suffering from advanced stages of psychosis with cerebral arteriosclerosis or senile psychosis. This treatment was administered with the thought that it would dilate cerebral blood vessels and improve the supply of oxygen to the brain. The infiltrations were made three to four times weekly. The patients underwent between 6 and 16 bilateral blocks over a period of several weeks. Using an anterior approach, a solution consisting of 12 cc. of 1 per cent procaine was injected into each ganglion. Each injection was followed by constriction of the pupils and narrowing of the palpebral fissures, but this syndrome disappeared in a few hours. Except for transient dizziness, no untoward complications were observed. Six patients in an advanced state of organic mental deterioration showed only temporary or moderate improvement. Two patients in the early phase of senile organic psychosis showed marked improvement. The improvement in one lasted for three months, but in the other it has been maintained for more than a year. It is tentatively concluded on the basis of these 2 cases that, although stellate ganglion block is not of great benefit to patients in the advanced stages of senile psychoses, it has beneficial effects in patients in the early phase of psychoses of late life. Its value in such patients should be further explored.

OSTEOPETROSIS IN ADULTS.

Hinkel, C. I., and Beiler, D. D. *Am. J. Roentgenol.* **74:** 46 (July) 1955.

Osteopetrosis usually occurs in childhood but is sometimes found in adults, it being discovered by radiographic means. In these instances, the benign form may have been present in childhood. A large percentage of the adult cases are familial, only siblings being involved. The disease is rarely seen in successive generations. Siblings usually have the same type of bone change but the severity of the disease may vary. The disease probably develops as the result of an hereditary trait which is governed by one or more genes of intermediate dominance. The essential defect appears to be inherent in the mesenchyme which is the common ancestor of hematogenic and osteogenic cells. The increase in density results from faulty resorption of endosteal and periosteal bone and matrix. Cartilage cells and unresorbed matrix are found in the bones of adults as late as the seventh decade. Osteopetrotic bones are increased in weight, fragility, and mineral ash content. In patients of this age, the dense inclusions are probably not viable. The clinical and roentgenologic characteristics on which diagnosis can be based are: The disease is generalized, although some bones may be spared. There is usually involvement of the posterior clinoids, spine, pelvis, proximal humeri and both ends of the femurs. There is pronounced symmetry of the lesions. The "bone within a bone" appearance is often seen in the pelvis, ribs, epiphyses, carpals and tarsals. There are usually transverse and longitudinal striations in the metaphyses. The vertebrae may present a "sandwich" appearance. Anemia is moderate or absent, seldom severe. The levels of serum alkaline and acid phosphatase, blood calcium, and phosphorus are essentially normal. Enlargement of the liver and spleen is uncommon. There is a predilection to fracture. There may be periodic or permanent remissions. The course is clinically benign. Five adult patients showing the changes characteristic of the disease are presented. The age at onset in these patients ranged from the prenatal period to about 4 years of age. There were several exacerbations and remissions but the osteopetrotic inclusions became enveloped by normal bone and the disease seemed not to be active.

ELECTROLYTE STUDIES IN HEART FAILURE. I. CELLULAR FACTORS IN THE PATHOGENESIS OF THE EDEMA OF CONGESTIVE HEART FAILURE.

Iseri, L. T.; Boyle, A. J.; Chandler, D. E., and Myers, G. B. *Circulation* **11:** 615 (Apr.) 1955.

Analyses of muscle for water, potassium and chloride were made in 10 cardiac patients during and after congestive heart failure. The potassium content per unit of wet tissue during failure was 30.1 per cent less than that during compensation. The concentration of potassium in the intracellular water increased from 116 mEq. per liter to 151 mEq. per liter with compensation. Calculated extracellular water decreased, but no change in intracellular water per unit of tissue solids was found. Eight of the 10 cases showed a decrease in chloride content; 2 showed an increase. The decrease in cellular potassium may possibly be due to osmotic activation of intracellular base which forces potassium out of the cells and/or absorbs water into the cells. (From authors' summary)

ELECTROLYTE STUDIES IN HEART FAILURE. II. EXTRACELLULAR FACTORS IN THE PATHOGENESIS OF CONGESTIVE EDEMA.

Iseri, L. T.; Mader, I. J., and Boyle, A. J. *Circulation* **11:** 620 (Apr.) 1955.

Variations in the plasma electrolyte concentration were studied in 10 decompensated cardiac patients before and after physical stress, and in 6 patients during the normal course of diurnal activity. A significant rise in the plasma sodium concentration was found, indicating an elevation of extracellular osmolarity. This was interpreted to reflect a rise in intracellular osmolarity. The pathogenesis of congestive heart failure is discussed in the light of these findings. (From authors' summary)

CARCINOMA OF THE MALE BREAST.

Jackson, P. P., and Munnell, E. R. *Canad. M. A. J.* **72:** 814 (June 1) 1955.

In physical examinations of the male, the breast should be checked for carcinoma just as frequently as in the female. The percentage of male breast malignancy represents from 0.87 to 2.9 per cent of total breast malignancy. The prognosis is considered extremely grave but it is not hopeless. A radical Halsted mastectomy with radical removal of the skin is recommended for all operable cases. Because of the size of the male breast, these carcinomas usually involve the skin very early and local recurrences are common. Twelve cases of malignancy of the male breast are presented. In each, the presence of a lump was the first thing noted. The patients ranged in age from 43 to 76 years. The symptoms had been present for periods of five weeks to five years. No common site of occurrence was noted. Four of the 12 patients had had a radical mastectomy ten years previously, and 2 of them were still living (10.5 and 11.5 years later, respectively). Three other patients in whom mastectomy was performed survived 8, 10 and 6 years, respectively, before succumbing to metastases.

THE CARDIOHEMODYNAMIC EFFECTS OF VENOUS CONGESTION OF THE LEGS OR OF PHLEBOTOMY IN PATIENTS WITH AND WITHOUT CONGESTIVE HEART FAILURE.

Judson, W. E.; Hollander, W.; Hatcher, J. D.; Halperin, M. H., and Friedman, I. H. *J. Clin. Invest.* **34:** 614 (Apr.) 1955.

During venesection or venous congestion of the limbs (acute reductions of "effective blood volume"), normal subjects, patients with compensated cardiovascular disease, and patients with cor pulmonale with or without failure had a fall in cardiac output. Patients with congestive heart failure due to valvular, hypertensive, or coronary heart disease usually had a slight rise, occasionally no change, or rarely a slight fall in cardiac output. The response in cardiac output was not necessarily accompanied by a change in the right ventricular end-diastolic pressure. A reduction in the pulmonary arterial pressure was not consistently observed. Decreases in cardiac output in some patients may explain the fall in pulmonary arterial pressure. (Authors' summary.)

LOCAL APPLICATION OF EPINEPHRINE TO CAROTID SINUS. LOWERING OF BLOOD PRESSURE AND MODIFICATION OF HYPERREACTOR RESPONSE IN HYPERTENSIVE PATIENTS.

Kezdi, P., and Hilker, R. R. J. *A. M. A. Arch. Int. Med.* **95:** 720 (May) 1955.

An experiment was undertaken in hypertensive patients, based on the theory that the failure of the sinoaortic regulatory mechanism to control hypertension may be the result of decreased pulsatile expansion of the arterial wall caused by relaxation and distension of the stretch-sensitive areas, resulting in less stimulation of the pressoreceptors. This in turn would allow a greater central sympathetic outflow, resulting in hypertension. By the local application of epinephrine, the wall of the carotid sinus would be contracted, its tension increased, and the normal pulsatile expansion restored. This would result in more inhibition of the central sympathetic outflow and the blood pressure would be lowered. The Valsalva maneuver, which tests the integrity of the sinoaortic regulatory system, was performed on 20 patients with essential hypertension in different stages of the disease. Twelve normotensive patients were also tested. Patients with hypertension had an exaggerated response to the Valsalva maneuver. In only 35 per cent of them did bradycardia develop, compared with 92 per cent of normal patients. The local application of epinephrine to the carotid sinus of hypertensive patients modified their hyperreactor response as measured by the overshoot in the Valsalva maneuver. It also lowered the blood pressure in all of the hypertensive patients by a significant amount, for periods up to three hours. The results indicate that the fundamental defect in essential hypertension may be according to the theory: increased sympathetic outflow caused by an impaired buffer nerve mechanism due to dilatation, abnormal relaxation and decreased pulsatile expansion (loss of elasticity) of the arterial walls.

THE RELATION OF AGE TO CERTAIN MEASURES OF THE PERFORMANCE OF THE HEART AND THE CIRCULATION.

Landowne, M.; Brandfonbrener, M., and Shock, N. W. Proc. 47th Annual Meeting Am. Soc. Clin. Investigation; Abstr., *J. Clin. Invest.* **34:** 948 (June) 1955.

Estimates of resting circulatory performance have been made in a series of 67 men clinically free of cardiovascular disease, aged 19 to 86. Peripheral resistance (R) increased with age, as shown by a decline in cardiac output measured by dye dilution, unassociated with a decrease in mean brachial intra-arterial pressure. With respect to the heart, there was an agewise decline in estimated external left ventricular work (W) at rest, since the increase in mean systolic pressure was not comparable to the decrease in stroke volume, and the heart rate decreased. The increase in estimated systolic duration implies a further decrease in power (P), *i.e.*, rate of work performance. Although the reduction in work may reflect lessened circulatory requirement, heart size did not diminish, and diastolic duration was increased. These indications of a decreased stroke work relative to diastolic volume specify a less favorable cardiac performance and therefore are evidences of a reduction in the reserve of the left ventricle as a muscular pump. Estimated effective central elasticity (E) showed a striking age correlation ($r = .76$), as the relative rate of decrease in pressure during diastole increased with age despite the increase in peripheral resistance. A residual individual variability in elasticity of ± 30 per cent limits the accuracy of predicting stroke volume from blood pressure curves by means of an age-dependent factor for elasticity.

STRUMA LYMPHOMATOSA (HASHIMOTO'S DISEASE).

Marshall, S. F., and Meissner, W. A. *Ann. Surg.* **141:** 737 (May) 1955.

Struma lymphomatosa is an uncommon disease of the thyroid. A series of 114 cases of struma lymphomatosa confirmed by operation and microscopic study is reported. It is a disease of women; there were only 2 males in the 114 cases. It may occur at any age, the average age being 50.2 years. The diagnosis is established by the clinical course of progressive enlargement of the thyroid, an elastic firmness associated with moderate pressure symptoms, and a lack of inflammatory reaction and of thyroid toxicity. The pathologic features, both gross and microscopic, are described. Treatment consisted of bilateral subtotal thyroidectomy in 82 cases and hemithyroidectomy in 25. It is suggested that bilateral resection best relieves pressure symptoms and prevents tracheal constriction. Operation is associated with no mortality and few postoperative complications. Surgical treatment is not necessary in all cases, and should be avoided if the diagnosis is definite when symptoms are mild. Postoperative hypothyroidism is common (70 per cent) and is permanent. Thyroid deficiency can be controlled by administration of desiccated thyroid, but treatment will be necessary throughout the patient's life. (From authors' summary)

CARCINOMA OF BARTHOLIN GLAND. REVIEW OF THE LITERATURE AND REPORT OF A NEW CASE IN AN ELDERLY PATIENT TREATED BY RADICAL OPERATION.

Masterson, J. G., and Goss, A. S. *Am. J. Obst. & Gynec.* **69:** 1323 (June) 1955.

The world literature containing 116 instances of carcinoma of the Bartholin gland is reviewed. This is a rare disease which has been reported with increasing frequency during the past ten years, perhaps because of more adequate diagnostic facilities. It is probably more common than the literature would indicate. Its reported incidence is approximately 1 to every 1,000 female genital carcinomas. A case report is presented of primary carcinoma of the Bartholin gland in an 83-year-old woman. She is thought to be the oldest reported patient to have undergone and survived a radical vulvectomy with inguinal, femoral and pelvic lymphadenectomy. This tumor should be treated in the same way as other carcinomas of the vulva. In general, they show a poor response to radiation. The radical surgical

approach is recommended as the treatment of choice. The prognosis should be favorable if adequate therapy is instituted early.

TRANSFERENCE AND RESISTANCE IN GERIATRIC PSYCHOTHERAPY.

Meerloo, J. A. M. *Psychoanalyt. Rev.* **42:** 72 (Jan.) 1955; through *Digest Neurol. & Psychiat.* **23:** 255, 1955.

Some old people show useful psychologic changes. Their rich experience may lead to inner wisdom, mental stability, and an ability to synthesize. Others, more anxious and rigid, cannot adjust to old age. One of the first signs of a breakdown in mental defenses is the return of emotions repressed in childhood, such as strong sexual wishes in formerly frigid and compulsive women, strong destructive and aggressive impulses in others, and repressed oral wishes in still others. The ego and ego defenses weaken, so that the old person may show increased sensitivity to environmental influences. Retirement from business, lowered income, and forced moving all may trigger neurotic or psychotic outbursts. The sudden death of a loved one, bringing conflicts relating to death to the fore, may cause a neuropsychosis. Many symptoms of elderly people are related to death, representing either passive surrender to, or denial of and flight from, death. The elderly person must also contend with a changed body image and increasing difficulties with body function. Psychotherapy, even of an analytical form, is possible in the elderly. The transference situation is different from that occurring with younger patients, the therapist often representing a child of the patient rather than a parent. For the most part, the patient transfers a combination of filial and parental images to the therapist. Old people often form a remarkably strong transference relationship; there is usually no indication for resolving this transference, which gives the patient social contact and replaces real losses of love and social appreciation. The goals of therapy with these patients are to give meaning to their past and to help them discover hidden inner resources. Resistances are handled differently from those in younger patients, since the older patient is already experiencing a breakdown of defenses. The therapist should not stir up the patient's emotions through continuous investigation of what the patient is unable or unwilling to communicate. Depressed patients in particular have a superego which is too severe, and the therapist has to play the role of a more benevolent superego and help the patient to be less regretful and punishing toward himself. Carefully chosen interpretations may have the same clearing value as in the psychoneuroses of younger patients. The therapist must be ready to work through problems of sexuality with his patients, who are usually frightened and ashamed to reveal them. In our culture, with its emphasis on the glamor of youth and rising success, there is no place for the aged. Elderly people are subjected to real trauma. Their treatment requires the cooperation of the general practitioner, social workers and welfare organizations.

RESULTS WITH A COMBINATION OF RAUWOLFIA AND ADRENERGIC BLOCKADE IN THE TREATMENT OF HYPERTENSION.

Moyer, J. H.; Hughes, W.; Dennis, E.; Beazley, H. L., and McConn, R. *Am. J. M. Sc.* **230:** 33 (July) 1955.

The hypotensive effects of Rauwolfia plus phenoxybenzamine and of these two agents combined with protoveratrine were compared in a series of 47 patients with varying degrees of hypertension. A significant hypotensive response (mean blood pressure reduction of 20 mm. Hg or more) was achieved in 82 per cent of 28 patients receiving the combination of the three substances. Of 19 patients receiving only Rauwolfia plus phenoxybenzamine, significant blood pressure response was obtained in 74 per cent but the latter group were patients with slightly more severe disease, in that all had previously been unresponsive to Rauwolfia alone. The side-effects of all regimens (including Rauwolfia alone) were seen in nearly all patients. The chief side-effects of the Rauwolfia-protoveratrine-phenoxybenzamine combination consisted of nasal congestion, sedation and fatigue, increased appetite, dizziness and bradycardia. Orthostatic tachycardia, a major side-effect of phenoxybenza-

mine alone, was seen infrequently when the drug was used in this combination. The dose requirement of phenoxybenzamine was greatly reduced as compared to that required with this agent alone. The results indicate that the combination of phenoxybenzamine and Rauwolfia, with or without protoveratrine, may prove generally useful in the treatment of all degrees of hypertension. Rauwolfia blocks vasoconstrictor impulses centrally, whereas phenoxybenzamine blocks vasoconstrictor impulses peripherally. Together these effects make this a potent combination for reducing blood pressure in patients with hypertension. (From authors' summary)

THE DIAGNOSIS OF CARDIAC HYPERTROPHY IN THE AGED: CLINICAL PATHOLOGICAL CORRELATIONS IN 55 INDIVIDUALS.

Rodstein, M. *Am. J. M. Sc.* **229:** 525 (May) 1955.

In an attempt to assess the accuracy of clinical methods of detecting cardiac enlargement or hypertrophy in elderly patients, the findings upon physical examination, chest film, and electrocardiographic examination in 55 men and women aged 63 to 95 years were correlated with observations at necropsy. The diagnosis of cardiac enlargement or hypertrophy was made correctly in 32 patients, all of whom showed moderate to marked hypertrophy of the ventricular muscle at necropsy. Slight hypertrophy of the ventricular muscle was demonstrated in 7 patients at postmortem examination, but was not detected by any of the clinical methods of examination. In 16 cases with no hypertrophy of the ventricular muscle at necropsy, 6 were diagnosed as showing cardiac enlargement on roentgenographic examination and 1 on physical examination. Cardiac dilatation was considered the probable basis for these diagnoses. None of this group manifested any of the electrocardiographic changes indicative of cardiac hypertrophy. In the 32 cases of moderate or marked hypertrophy of the ventricular muscle at necropsy, 20 were diagnosed by physical examination as showing enlargement; 19 of 24 were diagnosed by roentgenograms as showing enlargement; and 19 of 31 were diagnosed as showing cardiac hypertrophy by electrocardiographic criteria. The most sensitive electrocardiographic criteria for hypertrophy were RaVL greater than 11 mm. and R1 + S3 = 25 mm. or greater. This was attributed to the increased electrically horizontal position and counterclockwise rotation of the heart associated with aging. There was no consistent pattern of coexistence of diagnoses of enlargement or hypertrophy by the three methods, in the cases with moderate or marked hypertrophy of the ventricular muscle at necropsy. In these cases diagnoses of enlargement by roentgenogram and physical examination tended to occur more frequently in the same individuals than of either with hypertrophy by electrocardiographic criteria. This was attributed to the fact that the former are measures of size, whereas the latter is a measure of hypertrophy. In the cases with moderate or marked ventricular hypertrophy at necropsy, there was a larger number of patients showing enlargement in the roentgenogram and no positive electrocardiographic criteria of hypertrophy, than the reverse. This was attributed to the effects of the increased incidence of coronary and myocardial disease in this age group in diminishing the accuracy of the electrocardiographic criteria of hypertrophy. (From author's summary)

IMMEDIATE PARTIAL GASTRECTOMY FOR PERFORATED PEPTIC ULCER.

Rowlands, B. C., and King, P. A. *Brit. M. J.* **1:** 1254 (May 21) 1955.

Because of the inconvenience to patients of disabling symptoms in the period following simple suture, and of increased technical difficulties at a second operation, selected patients with perforated peptic ulcer were treated by immediate partial gastrectomy. The results in published series indicate that in experienced hands the mortality is probably no greater from immediate partial resection than from simple closure. The key to the successful use of the former seems to be in the selection of patients. The chief criteria for the selection of a patient fit for resection are: any perforated gastric lesion in a patient whose

general condition is good, large perforations, a history of previous perforation, and a long preceding history of ulcer dyspepsia, and concomitant hematemesis. The results of a follow-up study (Illingworth *et al.*) of 733 cases of perforation treated by simple suture are of interest in assessing the prognosis after perforation. Within five years, 70 per cent of the patients had a relapse, and 50 per cent had severe symptoms. The prognosis was worst in cases with a long antecedent history. The incidence of major complications, particularly reperforation and hematemesis, was 20 per cent within five years. Fifteen cases are presented in which partial gastrectomy was performed. There were 2 fatalities. The operation presented no technical difficulty and the postoperative period was uneventful.

TREATMENT OF INTRACTABLE PAIN WITH LARGE DOSES OF MORPHINE AND DIAMINOPHENYLTHIAZOLE.

Shaw, F. H., and Shulman, A. *Brit. M. J.* **1:** 1367 (June 4) 1955.

Morphine and its analogues have been only partially effective in relieving severe pain because doses sufficiently large to induce analgesia could not be administered without causing side-effects such as respiratory depression, tolerance, vomiting and constipation. This has been especially true in elderly and cachectic patients with poor hepatic and renal function. When 2:4-diamino-5-phenylthiazole hydrobromide (D.A.P.T.) is used along with morphine, doses large enough to induce satisfactory analgesia without associated undesirable effects can be employed. D.A.P.T. exerts marked and lasting antagonism against the respiratory depressant effect of morphine. It increases the depth of respiration but not the rate. It also apparently prevents or delays the onset of tolerance. It appears sometimes to antagonize the vomiting and, usually, the constipation associated with the administration of morphine. Therapeutic doses antagonize the respiratory depressant effect of morphine and, at an increased dosage, the substance also antagonizes the soporific effect of morphine. A still higher dosage may cause wakefulness and restlessness. Mental disorientation has been induced occasionally in elderly individuals. D.A.P.T. is a safe drug with a high therapeutic index. As large a dose as 100 mg. has been given without ill effect, but care in administration is advised when high dosages are reached. The usual dose is 15 mg. intramuscularly. D.A.P.T. has no analgesic properties, either orally or parenterally. Small doses have little effect on blood pressure but with a large dose (75 mg.) intravenously, the blood pressure may rise. It is recommended that the practice of giving small doses of morphine at frequent intervals for the control of severe pain be discontinued. The new plan of treatment, which is outlined, consists of giving gradually increasing amounts—that is, increments of ¼ gr. (16 mg.)—of morphine intramuscularly along with D.A.P.T. (15 mg.). The latter drug is given intramuscularly thirty minutes after the morphine when its maximum effect is being exerted. This treatment is continued until respiratory depression (or sedation) is evident, or an analgesia of from six to eight hours is obtained. If the degree of respiratory depression should cause concern, a dose of 10 mg. of D.A.P.T. intramuscularly may be repeated at ten-minute intervals, to a total of 60 mg. In cases of severe pain it may be necessary to give doses of morphine up to 2 gr. (130 mg.) three to four times daily along with D.A.P.T. When stabilization is reached, the intramuscular injection of D.A.P.T. is replaced by oral administration, a 20-mg. tablet being given simultaneously with the morphine injection. Special care must be exercised in the treatment of the aged. A barbiturate or hyoscine is usually given at night. When a patient has not received sufficient relief from a large injection (over 1 gr.) of morphine, the injection with D.A.P.T. may be repeated after two hours. If a patient's condition grows worse as death approaches and the period of analgesia becomes shorter, the dose of morphine may be increased by increments of ¼ gr. (16 mg.), but it is seldom necessary to increase the dose of D.A.P.T. The latter has almost no side-effects. Slight irregular flickers of the fingers, shoulder, and neck have been seen in some patients but could not be distinguished from similar movements in drowsy or deeply morphinized patients. There is no contraindication to the use of D.A.P.T. with hyoscine, atropine, barbiturate, chlorpromazine, or Marezine. The use of D.A P.T.

combined with morphine in 35 cases is reported. In about one-fourth of these patients a favorable change in outlook occurred during therapy. This aspect of the use of D.A.P.T. is still under investigation.

NONPARASITIC CYSTIC DISEASE OF THE LIVER.

Sifre, R. A.; Phelps, H. W.; Cole, N. J., and Kimball, C. H. *Ann. Int. Med.* **42:** 1288 (June) 1955.

A case of nonparasitic cystic disease of the liver is presented in which a preoperative diagnosis was made on the basis of x-ray studies of the upper gastrointestinal tract and gallbladder, which demonstrated the presence of an extrinsic pressure defect produced by one of the cysts. This is thought to be the first time such a defect has been demonstrated. These cysts usually are discovered only by their size. They have frequently been mistaken for other conditions such as hydrops of the gallbladder, ovarian tumors, or mesenteric, renal or pancreatic cysts, and the diagnosis has been established only at the time of surgery. The etiology of this condition has not been definitely established. When symptoms are present, they are usually due to pressure upon neighboring organs, hemorrhage into a cyst, torsion of its pedicle, inflammation, and rupture. The symptoms may be secondary to those associated with polycystic kidney disease. There may be pain in the right upper quadrant of the abdomen or in the epigastrium, nausea and vomiting secondary to pressure upon the stomach or duodenum, and jaundice. The pathologic features of nonparasitic cystic disease of the liver, which may occur in single or multiple form, are described. Treatment is surgical, the following procedures having been performed: aspiration, incision and drainage, marsupialization, partial or complete excision, and anastomosis of the cyst to the small bowel.

CARDIOVASCULAR AND RENAL RESPONSES TO THE COMBINATION OF HEXAMETHONIUM AND L-HYDRAZINOPHTHALAZINE (APRESOLINE®) IN HYPERTENSIVE SUBJECTS.

Stein, D. H., and Hecht, H. H. *J. Clin. Invest.* **34:** 867 (June) 1955.

Eighteen hypertensive patients were studied in order to evaluate the renal and cardiovascular adjustments to l-hydrazinophthalazine when given alone and after the administration of hexamethonium. The following observations were made: 1) l-Hydrazinophthalazine seemed to increase renal plasma flow only in patients with normal or nearly normal resting renal plasma flow. 2) The prior administration, parenterally, of a moderately hypotensive dose of hexamethonium, did not alter the ability of l-hydrazinophthalazine to increase renal plasma flow in some patients. 3) l-Hydrazinophthalazine caused an increase in cardiac output in all patients to whom it was given. 4) The prior administration of hexamethonium was capable of blocking the rise in cardiac output following the l-hydrazinophthalazine. (Authors' summary and conclusions.)

EFFECT OF ESTROGENIC HORMONE ON SERUM LIPIDS IN PATIENTS WITH CORONARY ARTERIOSCLEROSIS.

Steiner, A.; Payson, H., and Kendall, F. E. *Circulation* **11:** 784 (May) 1955.

The oral administration of 0.25 to 1.0 mg. of ethinyl estradiol daily to patients with coronary arteriosclerosis and to control subjects consistently produced a significant fall in the cholesterol-phospholipid ratio. This change was due to the lowering of the serum cholesterol level without much change in the phospholipid level in 5 of the 10 experimental periods. It was due to increased phospholipid levels without significant changes in the cholesterol levels in the other 5 instances. Serum neutral fat levels increased in 8 of the 10 periods studied. Toxic effects (fatigue, loss of appetite, nausea, vomiting, enlargement

and sensitivity of breasts, and loss of libido) of the estrogen prohibited its prolonged use, except as a tool for investigative study. There was no change in the incidence of chest pain or in the electrocardiogram in the patients with coronary arteriosclerosis during the period of observation. (Authors' summary)

REFLUX ESOPHAGITIS.

Stewart, J. D.; Chardack, W. M., and Alfano, G. S. *Ann. Surg.* **141:** 627 (May) 1955.

Reflux esophagitis is not uncommon and may result in dangerous and crippling complications. From a study of 66 cases, the etiologic factors were found to be: 1) incompetence of the cardio-esophageal sphincter mechanism, with sliding hiatal hernia or following a surgical operation, 2) gastric hypersecretion and the peptic-ulcer diathesis, 3) protracted vomiting, nasogastric intubation, or pyloric obstruction, 4) ectopic gastric mucosa as "short esophagus," or scattered islets, and 5) individual susceptibility. When symptoms can be controlled by a medical regimen with occasional dilatations, this is the method of choice. Surgery becomes necessary when the symptoms are not relieved and roentgenologic and esophagoscopic studies show the persistence or progression of esophageal inflammation and deformity, or if hemorrhage supervenes. The objectives of surgical treatment are: 1) prevention of the reflux of digestive secretions, either gastric or upper intestinal, into the esophagus, 2) promotion of rapid drainage of the esophagus and the part of the alimentary canal into which it empties, 3) reduction of gastric acidity to a low value, or the production of anacidity, 4) relief of esophageal obstruction, and 5) exclusion of the possibility of neoplasm of the esophagus. Various operations were carried out among the 66 patients. A plan for surgical treatment was evolved. The repair of hiatal sliding hernia is of utmost importance. It should usually be accompanied by gastric resection. This is necessary if the diaphragmatic tissues are such as to render repair of the hernia insecure, if it is not possible to reduce the cardio-esophageal junction to its normal position, or if there is clinical evidence of duodenal ulcer. Such remedial surgery should be performed before the esophagus has become fibrotic and shortened. The most difficult problem peptic esophagitis poses is how best to restore continuity of the alimentary canal after the lower esophagus has been resected because of fibrotic stenosis and shortening. The most satisfactory plan seems to be to resect as much of the proximal stomach as possible and leave enough distal stomach to bring into the chest for esophageal anastomosis. Pyloroplasty is added to the procedure to promote rapid gastric emptying. Some success has been achieved with esophagojejunostomy according to the Roux Y principle, with or without gastrectomy, but this procedure is not as applicable under varied anatomic conditions.

THE EFFECT OF HEPARIN ON THE CEREBRAL BLOOD FLOW OF ELDERLY STATE HOSPITAL PATIENTS.

Talley, R. W. *Am. J. M. Sc.* **230:** 61 (July) 1955.

Heparin was used for its effect on the lipoprotein, chylomicron and neutral fat content of serum in 11 elderly patients, in an attempt to increase the cerebral blood flow. All of the patients had a significantly lower cerebral blood flow and cerebral oxygen utilization, and a significantly elevated cerebral vascular resistance as compared with normal control patients. Studies after the administration of heparin in doses of 200 mg. intravenously showed no significant change in any of the determinations and there was no obvious improvement in mental ability. Because of the possibility that patients who had had an obvious stroke and those with senile dementia might respond differently, 6 patients with cerebrovascular accidents were compared with 5 in whom no history or evidence of a cerebrovascular accident was obtained. No significant difference was noted either in the pretreated or treated groups.

BACTERIAL ENDOCARDITIS IN THE AGED.

Wallach, J. B.; Glass, M.; Lukash, L., and Angrist, A. A. *Ann. Int. Med.* **42**: 1206 (June) 1955.

In a review of several groups of patients with bacterial endocarditis reported in the literature, from 15 to 50 per cent of the cases were found to occur in patients over the age of 50 years. Bacterial endocarditis was present in 82 (16.1 per cent) of 509 patients with rheumatic heart disease (Group I) whose necropsy records were reviewed at the Queens General Hospital, and in an additional 47 patients in whom the hearts did not meet the criteria for rheumatic heart disease (Group II). Thirteen patients in Group I and 17 patients in Group II were more than 50 years of age. Seven cases in Group I and 13 in Group II were acute. The pathogenesis of bacterial endocarditis represents an infection of nonbacterial thrombotic lesions on the valves, which tends to occur on those in which the collagen has become dense and fibrous. In younger individuals the predisposing cause of this collagen change is rheumatic valvulitis, but with increasing age the degenerative changes of senility and other degenerative diseases play an important role. Thus, older patients with acute endocarditis more frequently showed genito-urinary infection, diabetes, bronchopneumonia, a postoperative status, or sclerotic changes in the valves. The metabolic defect of the aging process in the collagen makes the valve particularly susceptible to stress and this favors the formation of the nonbacterial thrombotic vegetation. The associated breakdown of immunity favors invasion of the blood stream by infecting organisms. In the older patient the endocarditis is more often of the acute type. The cases are likely to be of the ulcerative rather than of the vegetative type. In younger individuals *Streptococcus viridans* is likely to be the causative organism, whereas in the elderly the bacteriology is likely to include a wide range of organisms. Fewer glomerular lesions are found in elderly patients, probably because there is less time for their development and because of a diminished tendency on the grounds of immunity and reactivity for the development of glomerular lesions. In older patients, bacterial endocarditis often represents only an incidental terminal infection of a fresh nonbacterial thrombotic vegetation and plays little part in the mechanism of death of the patient. In contrast, the disease in younger patients is usually the cause of the illness and death of the patient.

NEWS AND NOTICES

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS

The Annual Meeting of the American Society for the Study of Arteriosclerosis will be held at the Palmer House, Chicago, *November 11 and 12, 1956*. The program and abstracts of all of the papers to be presented will be published in the October issue of *Circulation*.

For further information please write to Doctor R. Gordon Gould, Program Chairman, P. O. Box 1663, Los Alamos, New Mexico, or to Doctor O. J. Pollak, Secretary-Treasurer, P. O. Box 228, Dover, Delaware.